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Calcification of the Left Annulus Fibrosus

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CALCIFICATION of the left annulus fibrosus is a not infrequent autopsy finding in old individuals. The lesion seems to have been first described in 1910 by Dewitsky (1) and has subsequently been studied in greater detail by Ribbert (11), who stated that the left annulus can be changed into a calcified ring. Among later publications on the subject, those by Geerling (4), Martens (8), Ipsen (7), Epstein (2), Geill (5), and Rytand and Lipitch (12) should be mentioned. The present investigation deals chiefly with the pathologic and anatomic changes observed in calcification of the left annulus fibrosus but will include also observations on the symptomatology of this disease.

FREQUENCY, AGE, AND SEX DISTRIBUTION

In the present communication a survey of the incidence of the annulus calcification among the inmates of De Gamles By in Copenhagen will be given. This institution is administered by the municipality of Copenhagen and has a population of about 1600 persons who are all recipients of old age assistance. About one-half of the patients are inmates in the hospital or infirmary divisions of the institution. The number of autopsies performed yearly is approximately 500, the majority of the patients dying in the institution coming to autopsy.

During a period of eight years 230 cases of calcification of the annulus fibrosis were observed at autopsy, 196 occuring in women and 34 in men. The percentage incidence is respectively 9.4 and 2.7. The distribution within the various age classes is given in table 1.

TABLE 1. CALCIFICATION OF THE LEFT ANNULUS FIBROSUS (DISTRIBUTION ACCORDING TO AGE AND SEX).

Age	Women (196 Cases)	Men (34 Cases)
60—69	14	2
70—79	57	12
80—89	108	15
90—99	17	5

The incidence of annulus calcification increases with advancing age. Thus in the age group 80 to 89 this condition was found in 12 per cent of the women and 3.2 per cent of the men.

THE ETIOLOGY OF THE ANNULUS CALCIFICATION

The etiology of the calcification of the left annulus fibrosus and particularly the cause for the much more frequent occurrence of this lesion in women remains unknown. It is unlikely that there is any direct correlation between arteriosclerosis and calcification of the annulus when one considers that arteriosclerosis occurs predominantly in men whereas calcification of the annulus is found with much greater frequency in women. An evaluation based on the autopsy material from De Gamles By shows an increase with age both of the arteriosclerosis of the aorta and coronary arteries and of the incidence of annulus calcification, but the data fail to show any direct correlation since one often observes advanced arteriosclerosis in patients with slight annulus calcification, and vice versa.

Dr. Geill, after receiving his M.D. degree from the University of Copenhagen in 1921, continued his studies at Vienna and Paris. He has been chief physician of De Gamles By since 1936. Dr. Geill is President of the Danish Gerontological Society, and his chief research subjects are gerontology, cardiology, and vitaminology.

Martens (8) has emphasized the frequent occurrence of annulus calcification in connection with hyperostosis of the frontal bone and calcification of the intervertebal discs and the same author believes that changes, especially in women, in the calcium metabolism in connection with tissue damage are of importance in the development of the annulus calcification. Ipsen (7) calls attention to the possibility that endocrine factors are of etiologic significance since the disease predominately occurs in the female. In favor of the theory of the existence of disturbances in the calcium metabolism is the fact that extensive senile osteoporosis (senile osteomalaica), manifesting itself by the well-known senile kyphosis occurs with great frequency in old women. It may be assumed that the large amounts of calcium mobilized from the bones are deposited among other places in the left annulus fibrosus, whereas certain degenerative tissue changes (Dewitzky's annular sclerosis) provide especially favorable conditions for the deposition of calcium.

It should be mentioned that Rytand and Lipitch (12) in a few cases of annulus calcification have observed elevated values of serum proteins and serum cholesterol. The coexistence of the blood changes and the annulus calcification is probably only coincidental.

It is stated in many textbooks and publications that annulus calcification occurs with particular frequency in those instances in which a mitral endocarditis has previously been present, as evidenced by a thickening of the free valvular margins, valvular contraction, and fusion of the chordae tendineae. According to this contention, the annulus calcification represents merely a secondary phenomenon in relation to the previously healed endocarditis. Dewitsky (1), however, has established the annulus calcification as an independent disease developed on a purely degenerative, non-inflammatory basis. Fishberg (3) likewise states that annulus calcification may occur in individuals who do not show signs of any previous endocarditis.

In the autopsy material studied in this publication residuals after previous mitroendocarditis could be observed only in 14 of the 230 cases of annulus calcification. In these figures are not included a few cases of terminal endocarditis, since this condition is without significance for the problem under consideration. It is consequently permissible to draw the conclusion that the calcification of the left annulus fibrosus is an independent disease in old individuals and is not secondary to a previous endocarditis.

Pathologic Anatomy

The degree of the calcification varies considerably. In the slightest degrees one finds at autopsy a small tissue calcification, less than a pea in size, and generally situated in the posterior part of the annulus fibrosus, corresponding to the attachment of the posterior cusp. In more advanced cases the calcification extends through larger sections of the annulus and in the severest cases the whole annulus is changed into a solid calcified ring up to 1 cm. in thickness. In rare instances the calcification may assume monstrous forms. Thus figure 1 shows the roentgenogram of an isolated heart in which the annulus calcification presents the shape of an irregular calcified ring several centimeters thick. The severest degrees of calcification are usually found in women. From the calcified annulus, projections may radiate into the anterior and posterior wall of the heart and into the septum. In most instances the condition consists of a simple deposit of calcium salts. But Dewitsky (1) has reported two cases in which true bone tissue has been found. Kiær, the pathologist of De Gamles

FIG. 1. Monstrous calcification of left annulus fibrosus (Roentgenphotograph of autopsy specimen).

By, has in some instances carried out histologic examinations of tissue sections from the annulus calcifications prepared after decalcification of the tissue. The histologic examinations showed closely grouped crystals, which in size, shape, and color corresponded to calcium crystals, but in no instance was bone tissue observed. Those parts of the myocardium which were adjacent to the calcified masses showed signs of pressure atrophy with the development of large, irregularly shaped fibrous tracts of connective tissue splitting the muscular bundles. In severe cases calcified masses were seen to invade the myocardium.

CLINICAL ASPECTS

The symtomatology of the annulus calcification has been the subject of very few investigations. This is explainable by the fact that the disease is only very rarely recognized in vivo and because the clinical manifestations are not very pronounced.

The roentgenologic demonstration of the annulus calcification is difficult because the blood contained in the heart often obscures the calcification. By examination in the right oblique diameter it will, however, frequently be possible to demonstrate the annulus calcification in vivo (Odquist, 10). Most frequently the diagnosis will remain a probability diagnosis.

The question of to what extent the annulus calcification is capable of producing a mitral stenosis has been the subject of some discussion. Most frequently the stenosis must be characterized as slight (Fishberg, 3; White and Bland, 14). It should be mentioned that the test for the diagnoses of the existence of a stenosis, namely, inability to pass two fingers through the mitral opening is very uncertain. The same holds true for the demonstration of a dilated right atrium since the presence of the auricular fibrillation is frequent in old individuals. Thus auricular fibrillation was found in not less than 10 per cent of all hospitalized individuals in De Gamles By. A more certain criterion for the existence of a mitral stenosis is the actual circumference of the mitral ostium, as measured on the ostium cut open. According to White (13) the circumference of the normal ostium is 9 to 11 cm. and only measurements below 7.5 cm. can be characterized with certainty as mitral stenosis. The criteria set forth by Wanscher, the present pathologist of De Gamles By, are even more exacting, since according to him, the circumference of the mitral ostium must be below 7 cm. in order that a diagnosis of mitral stenosis can be made with certainty. Even this numerical basis for the diagnosis of mitral stenosis should be considered as only approximate since the varying body size of individuals is not considered in the evaluation. It has, however, not been possible to make any corrections for body size.

It will be seen from table 2 that when Wanscher's criterion is used the annulus calcification has caused a mitral stenosis in only 5 cases. If, on the other hand, White's definition of mitral stenosis is used the number of cases of mitral stenosis is increased to 19. In all instances the mitral stenosis produced by the annulus calcification must be characterized as

TABLE 2. CIRCUMFERENCE OF MITRAL OSTIUM.

Centimeter	Number of Cases
6	3
6½	2
7	19
7½	18
8	51
8½	18
9	41
9½	12
10	22
10½	4
11	7
11½	1
	Total 198

only slight. In this respect, this type of mitral stenosis distinguishes itself clearly from the often very considerable degree of stenosis, for instance, the button-hole stenosis which occurs following rheumatic fever. In concordance with this, the mitral stenoses accompanying annulus calcification do not produce any considerable functional disturbance. The patients do not die as a consequence of the mitral stenosis, but this lesion is as a rule only an incidental finding at autopsy.

Of greater clinical importance are the calcium masses which invade the myocardium from the calcified annulus. It was already shown by Mönckeberg (9) that such invasion into the interventricular septum is capable of producing disturbances of conduction. Among the 8 patients studied by Geerling (4), 1 had a complete atrioventricular block and out of 10 patients observed by Rytand and Lipitch (12), 5 likewise had a complete atrioventricular block which, however, in one instance was only intermittent.

In my own material invasion by calcified masses from the annulus into the myocardium was found in 11 cases. In 5 of these cases the interventricular septum was invaded, in 1 case both the septum and the posterior wall of the heart, in 1 case both the anterior and posterior walls, and in the remaining 4 cases the posterior wall alone.

In table 3 a survey is given of the electrocardiographic changes observed in the 11 cases of annulus calcification associated with invasion of the myocardium. Of the 5 patients in whom calcified masses in the septum were found, 2 had a complete atrioventricular block which had been present for at least 5 years. The calcified tissue masses in these cases had a length of 2 to 2.5 cm. In 2 additional cases a beginning and a completely developed bundle branch block of Wilson's type was found. In the fifth case, in which the calcified tissue extended to below Tawara's node, the patient had had attacks of paroxystic ventricular tachycardia of the malignant type.

TABLE 3. ELECTROCARDIOGRAPHIC CHANGES OBSERVED IN 10 PATIENTS WITH EXTENSION OF CALCIFIED MASSES INTO MYOCARDIUM.

Location of Calcified Masses	Electrocardiographic Findings
1. Septum	Total atrio-ventricular block
2. Septum	Total atrio-ventricular block
3. Septum	Wilson block. Enlargement of Q_3
4. Septum	Incipient Wilson block. Auricular exstrasystoles.
5. Septum	Paroxystic ventricular tachycardia
6. Septum and posterior wall	Isoelectric T_1
7. Posterior wall	Auricular fibrillation. Ventricular exstrasystoles. Wide initial ventricular complexes
8. Posterior wall	T_2 nearly isoelectric. Enlargement of Q_3
9. Posterior wall	Diphasic T_1. Inversion of T_2. Auricular exstrasystoles
10. Posterior wall	P-Q interval 0.32 seconds. Auricular exstrasystoles.

There does not remain any doubt, therefore, that invasion of the interventricular septum by calcified tissue is capable of producing conduction disturbance ranging from the lightest to the severest degrees. In the remaining cases in which the calcified tissue extended into the anterior and posterior wall of the heart various myocardial changes were demonstrated including abnormalities of the t-waves, deep Q_3, auricular fibrillation, and exstrasystoles. It is, however, not possible to observe any definite correlation between the presence of the calcified tissue projections and the observed electrocardiographic changes, for which reason it seems likely that they must be considered as an incidental finding.

The author has finally attempted to clarify the significance the presence of annulus calcification has for the development of heart murmurs. It is well known that heart murmurs, ranging in intensity from slight to very marked, can be heard with remarkable frequency in old individuals both over the aortic and apical regions. The findings at autopsy showed that the causes for such murmurs can be very different. Besides being produced by valvular disease on an endocarditic basis, the murmurs may be caused by calcification of the aortic valve or the left annulus fibrosus, but not infrequently one finds at autopsy no organic changes which can explain the murmurs. One is therefore obliged to characterize such murmurs as functional, which only means that the etiology of the murmurs is unknown.

In order to delimit a group of patients with calcification of the annulus fibrosis as the only cause of the murmurs, the author in the present autopsy material excluded all cases in which signs of previous endocarditis or calcification of the aortic valves were found. Out of the 230 cases there remained then 176 in which the annulus calcification was the only macroscopic finding. For comparison with this group a control material of 176 individuals showing the same distribution with regard to sex and age was selected. The autopsy in none of these cases demonstrated the presence of disease of the cardiac valves or ostia, including annulus calcification. Table 4 shows the occurrence of heart murmurs in the two groups. In the group with annulus calcification murmurs occured in slightly less than two-thirds of the patients, and in the control group in slightly less than one-third. In the first group the heart murmurs were usually more pronounced and particularly rough, and diastolic murmurs were found with considerably greater frequency than in the control group.

In some cases of annulus calcification in which stethoscopic examination had revealed the presence of presystolic murmurs, which were further verified by phonocardiography (fig. 2) the autopsy unexpectedly revealed no certain stenosis of the mitral ostium. It must therefore be assumed that the blood stream during its passage from the left auricle to the left ventricle in the presystolic period causes the calcified mitral ring to vibrate and that

TABLE 4. HEART MURMURS OBSERVED AT THE APEX OF THE HEART.

Intensity of Murmur	Number of Cases	
	Calcification of Annulus	Control cases
No murmur	77	121
Slight murmur	27	29
Moderately intense murmur	59	21
Murmur of marked intensity	13	5
Total	176	176
Character of Murmur		
Systolic	63	37
Rough and diastolic	36	18
Total	99	55

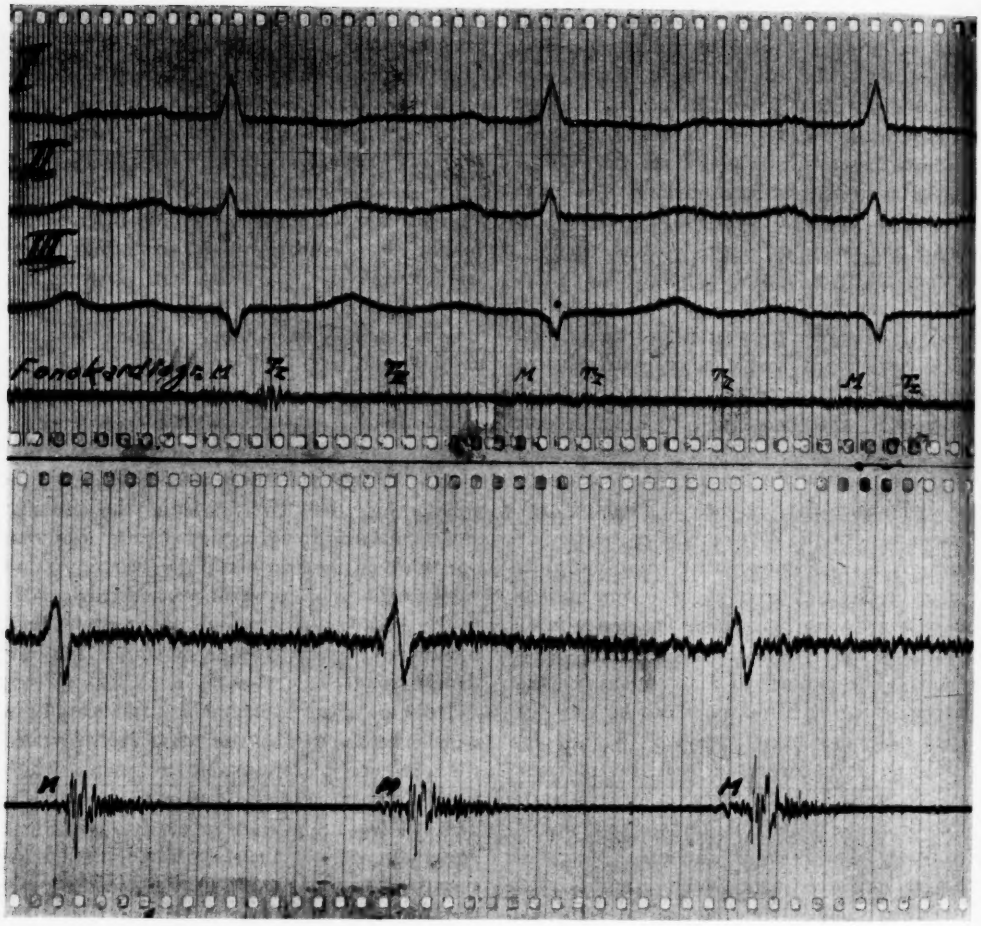

FIG. 2. Phonocardiograms from two patients show late diastolic murmurs. At autopsy annulus calcification without mitral stenosis was found.

this is the cause of the observed murmur. It seems therefore that in old individuals one has to consider this the mechanism for the production of the diastolic murmurs observed in the apical region. It should be added that under the same conditions it is frequently possible to demonstrate the presence of a marked thrill over the apical region.

SUMMARY

On the basis of 230 observed cases of calcification of the left annulus fibrosus, a correlation of various clinical, pathologic, and anatomic findings has been made. It is concluded that calcification of the left annulus fibrosus must be considered as a geriatric entity. The disease occurs predominantly in women, the incidence as observed in autopsies of women over 60 years of age being 9.4 per cent as compared with only 2.7 per cent in men above this age. The annulus calcification constitutes a disease by itself independent of the existence of a previous mitral endocarditis. The simultaneous occurrence of these two diseases must there-

fore be considered as coincidental. Even though the calcification may obtain considerable degrees and may convert the left annulus into a centimeter thick calcified ring, the lesion only in a few instances produces a mitral stenosis and then only in a mild degree.

From the annulus calcification calcified tissues masses may extend into the myocardium but only in the rare instances in which the interventricular septum is invaded do myocardial complications in the form of conduction disturbances develop.

In approximately two-thirds of the patients with annulus calcification the presence of heart murmurs was demonstrated, whereas such murmurs were found in only about one-third of the patients without annulus calcification. The heart murmurs associated with the annulus calcification were very frequently diastolic and possessed a rough character. Since in many instances it is not possible to demonstrate mitral stenosis at autopsy, the cause of these murmurs must be sought in the passage of the blood from the left auricle to the left ventricle during the presystolic period, by which passage the calcified annulus is made to vibrate.

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An Interpretation of the Calculated Changes in Renal Resistance with Age

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THE decrease in renal blood flow observed in individuals over the age of 50 (1) is unaccompanied by a decrease in blood pressure. On the contrary, mean blood pressure increases with age (7). While neither a decrement nor increment in cardiac output has been demonstrated (5), the alterations in flow and pressure suggest an increase in the resistance of the renal vasculature, even to a degree greater than might occur overall in the rest of the circulatory system.

Augmented values for renal resistance in an older group of subjects have been reported from this laboratory (6). In the same study renal hyperemia has been shown to result from pyrogen administration in the older, as well as the younger subjects, and resistance calculations were presented which indicate that a significant vasodilation can occur regardless of age. The following report is concerned with an analysis and interpretation of these estimates of renal vascular resistance.

The expressions which purport to show the renal resistances for the three age groups are based upon Lamport's formulae (4). The pertinence of these formulae to the material studied depends upon the validity of certain assumptions which are involved.

Certain components of the formulae may be altered in older subjects. Not only were blood flow, blood pressure, osmotic pressure, and filtration fraction altered, but changes in serum protein and hematocrit were noted, indicating a change in blood viscosity, and in accordance with Lamport's suggestion, have been dealt with by the use of "hydraulic" resistances.

Of relatively less importance is the consideration that certain other parameters used in the formulae are assumed to be constants, but might change with age. If either intrarenal pressure or "yield" pressure rose in the older subjects, true resistance would be lower than that obtained by use of the assumed constants for these pressures. However, an increase in intrarenal pressure sufficient to vitiate the calculated increase in afferent resistance would lead to an intrarenal pressure in excess of estimated filtration pressure. The use of an average of auscultatory systolic and diastolic brachial blood pressures for mean aortic or renal arterial pressure would not appear to be of equal validity for old and young subjects. In older subjects pressure contours are altered, auscultatory pressures are less reliable, and brachial-renal correspondence is not established.

In the strict sense these formulae are not expressions for arteriolar resistance alone, but apply to a larger vascular segment. The term for afferent resistance, while usually assumed to refer to the afferent arteriole predominantly, is more correctly an expression which, as defined, approximates the total vascular resistance of a segment between the aorta and an equilibrium filtration point on the glomerular capillaries.

In the young normal individual the glomerular afferent arteriole may contribute most of this resistance, but such may not be the case under all circumstances of age and/or disease; therefore, the calculated increase in R_a in the older subjects represents only a rise in the resistance of the circuit included. It cannot define the specific anatomic site of this augmentation which might well be in the aorta or renal arteries. The term "afferent arteriolar resistance," therefore, should not be used in this instance. The same considerations apply to the formula for the efferent renal resistance. Here, however, the changes which have been noted in older kidneys do not suggest that the efferent arterioles make relatively less contribution to

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the resistance of this segment, and the term, "efferent arteriolar resistance," may be appropriate for description.[1]

In a branched circulation, change in resistance can occur in various ways. Any increase in calculated resistance represents a net figure and does not indicate the manner in which this is achieved. It could be the result of a reduction in the number of renal branches without change (or even with a decrease) in the resistance of each branch. It could be due to decrease of the vascular calibre without obliteration. Probably a reduction both in number of branches and in vascular lumen occurs with increasing age. This relation may be schematically described by a simplified analogue, where the renal circulation is considered as a circuit with n branches in parallel. Each branch corresponds to a renal circulatory unit with resistance $u_1, u_2, \ldots u_n$. Each unit is composed of afferent and efferent segments, and each segment possesses a fixed and a variable component. While the resistance of each branch is not the same, one may substitute an equivalent circuit with n branches but with equal branch resistances U. The resistance (Ω) of such a parallel circuit will be U/n. If an increase in cross sectional diameter occurs, the resulting amount of change in resistance will depend upon whether this is accomplished by the addition or opening up of new units or by dilatation of patent units—or by both. For our purpose peripheral resistance is considered to ex-

[1] Since this paper was written, Dr. Homer W. Smith has kindly made available to us a portion of the manuscript for his new book containing Gomez' most recent formulae. These propose somewhat different definitions for the renal vascular segments. Corrections are not made for differences in blood viscosity; the data for our older subjects indicate a reduction in viscosity which tends to reduce the effect of an increase in frictional resistance. Mean brachial pressure still defines the proximal end of the afferent segment as in Lamport's formulae. The termination of this segment is, however, defined by Gomez by the glomerular pressure. Our data do not enable us to determine whether the glomerular pressure values as estimated from either Gomez' or Lamport's formulae are equally valid in young and old subjects. Efferent resistance becomes proportional to filtration fraction by assuming a constant glomerular capillary permeability. This probably reduces the computed resistances for the defined vascular segment, R_E in the older subject. When recalculated by the Gomez formulae our data show little difference between young and old in residual efferent resistance after pyrogen administration, due to the identity of filtration fraction. This would limit our estimates of vascular obliteration to 5 per cent, so that the change in afferent resistance induced by pyrogen, and the resistance remaining after pyrogen would show an even greater increase with age. For these reasons we have left our results in terms of Lamport's formulae.

press frictional loss, which is proportional to the length divided by at least the fourth power of the radius.[2]

In our biologic system we shall assume that n can decrease (by obliteration of vessels) but it cannot increase. U may increase (reduction in lumen) or decrease (dilatation of lumen). Since failure to consider obliteration of vessels (decreased n) would in itself result in a calculated increase in unit resistance, some estimate of the degree of this obliteration is necessary before the data can be interpreted to indicate the average change in the individual circulatory unit.

Each unit is considered to be composed of an afferent and an efferent segment in series. The juncture of these is defined by certain arbitrary criteria (4) which in general serve to separate the circuit about an assumed point of filtration equilibrium in the glomerulus. The number of afferent branches (n_a) may equal or exceed the number of efferent branches (n_e) since, as defined, functional loss of the efferent segment does not require loss of the afferent path. Any afferent loss requires the concomitant nonperfusion of the efferent unit in continuity with it, so that n_a cannot be less than n_e.

[2] This is not quite true. For several reasons (2, 3) the resistance of blood vessels in the body is not independent of the pressure but decreases with pressure approximately in exponential manner. On this important consideration we have no pertinent information. It can be safely omitted from the rest of this analysis since including this factor would merely exaggerate the differences otherwise obtained. Assuming equal proportionality constants for all ages minimizes the differences in resistances and radii calculated from the above formula. However, the use of equal exponents for both groups is more likely to overestimate the radial dimensional difference, since a higher than fourth power exponent might be more applicable in the older group.

The vascular response to pyrogen was selected as a measure of the variability of calibre of the segment. The lowest resistance value after pyrogen is therefore taken as an estimate of the largest diameter achieved. The resistance after pyrogen is assumed to relate to the fixed or structural characteristics of the vessel at a given pressure. Since we do not know whether or not the vessels are capable of greater dilatation, our estimates of structural or fixed resistance may be high.

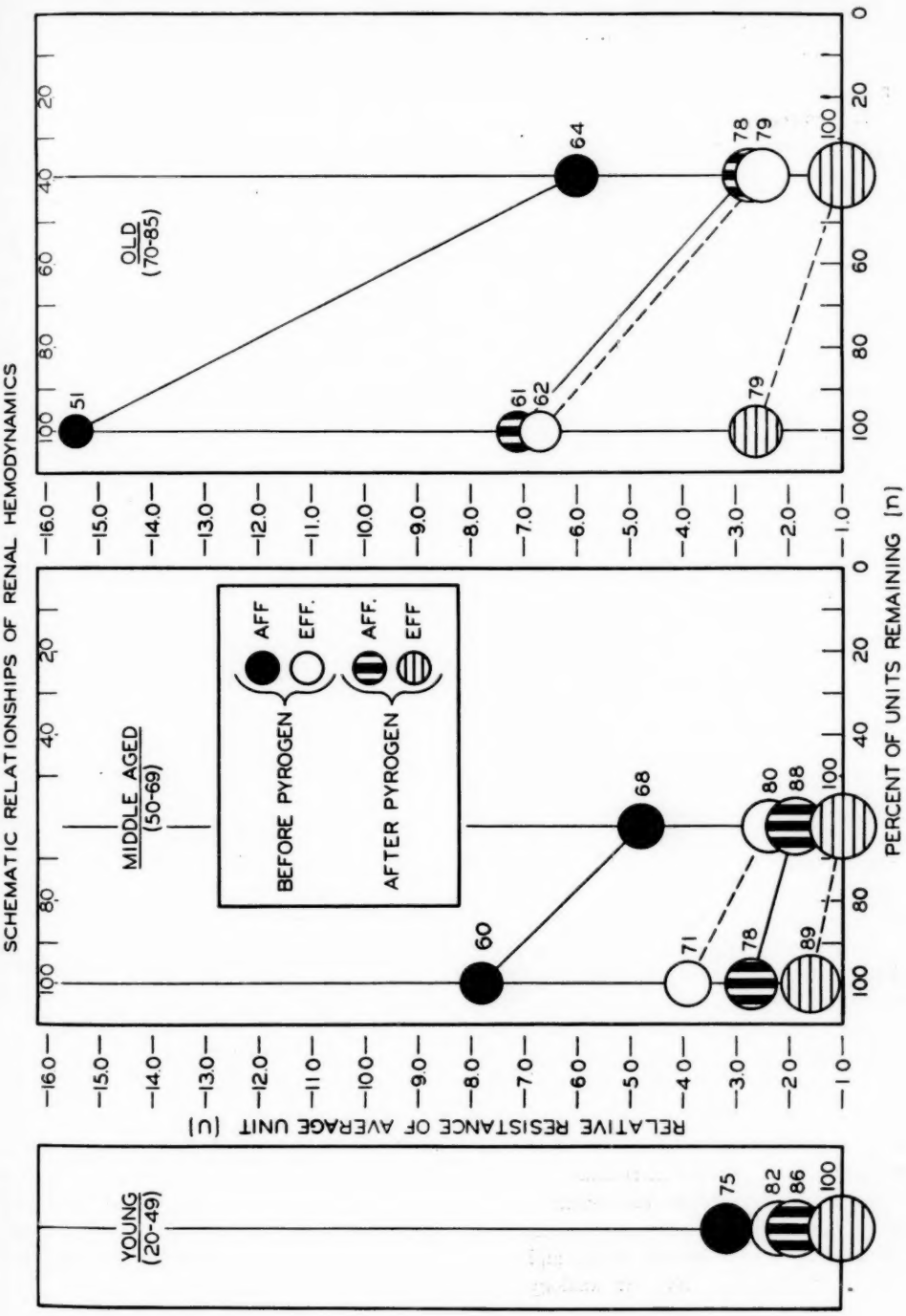
The resistances before pyrogen, therefore, are composed of this fixed component plus a variable resistance or vasoconstriction. For both the fixed and variable components of the circuit, n will be the same; since for a given unit U per branch, a loss of variable resistance will result in increase in the fixed resistance.

In figure 1 an attempt is made to indicate certain possible idealized relationships. The abscissae indicate the relative number of vascular unit branches. These are considered to be 100 per cent for the young subjects (Y group). For the old (O) and the middle (M) groups two limiting conditions are represented: a) if there were no vascular obliteration (n = 100 per cent) and b) for the greatest reasonable reduction in n. The latter values of n (38 per cent for O, 59 per cent for M) are chosen to make the corresponding efferent fixed unit resistance equal to that of the Y group. Any lesser n in the O or M groups would predicate a reduction in efferent fixed unit resistance with age, and this is unlikely. Values for intermediate degrees of vascular obliteration lie along the diagonal lines connecting the pairs of circles representing the limiting conditions.

The n_e determines the minimal n_a. The or-

FIG. 1. Schematic concept of the relation between the number of renal circulatory units and the state of the functional segments of each unit. Ordinate indicates resistance units divided by 2.0×10^3 mm. Hg (min./cc.) (body surface $m.^2/1.73\ m.^2$), the value for the efferent resistance after pyrogen administration in the young group. In comparison with the young group unit resistance values for the middle and old groups will vary depending upon the relative number of functioning unit branches indicated on the abscissa. See text for discussion.

SCHEMATIC RELATIONSHIPS OF RENAL HEMODYNAMICS


SCHEMATIC RELATIONSHIPS OF RENAL HEMODYNAMICS
RELATIVE RESISTANCE OF AVERAGE UNIT (U)
PERCENT OF UNITS REMAINING (n)
YOUNG (20-49)
MIDDLE AGED (50-69)
OLD (70-85)
BEFORE PYROGEN
AFTER PYROGEN
AFF.
EFF.
AFF.
EFF.
75
82
86
100
60
68
71
78
80
88
89
100
51
64
61
62
79
78
79
100

dinate scale indicates the resistance in Lamport's units divided by 2.0, which is the efferent resistance remaining in the young group after pyrogen administration. This efferent value is thus selected as an arbitrary reference point and assigned a relative resistance of 1.00 and radius of 100. The relation between the afferent and efferent values for resistance for corresponding values of n are indicated by the position of the black and white circles, respectively. The sizes of the circles suggest the relative lumen of the idealized vessel of unit length which would offer this resistance, with the relative radius indicated alongside. The solid black and open white circles indicate the base line (resting) condition. The barred circles are based on data obtained after pyrogen administration and are considered to reflect predominantly the structural resistance and dimensions. The changes effected by pyrogen are expressed by the differences in position and size of the homogenous and barred circles.

The kidney representative of the O group may in this manner be characterized by a reduction of up to about 60 per cent in the number of its vascular branches. In addition, in at least the afferent segment, comprising the vessels leading to as well as those within the kidney, structural change has occurred. The average resultant structural resistance in each branch, consequent to an effective radial narrowing of from 8 to 28 per cent, has increased by 45 to 275 per cent. The structural resistance has thus become as great or greater than the total effects of the combined structural resistance and vasoconstriction in the young. Nevertheless, an additional element of afferent vasoconstriction persists in the O group. This is supplied by a degree of radial shortening comparable to that manifest by the young.

The effect of equidimensional vasoconstriction in the O group is to produce a disproportionately high increase in resistance so that the component ascribed to vasoconstriction as well as the structural component of afferent renal resistance both become much higher in these older subjects. By our analogy, this structural change is not effectively compensated for by any reduction in the radial shortening or in the vasoconstrictive resistance increment.

With regard to the efferent vessels, there may or may not be structural alteration in the individual idealized unit. If such is present, the maximum resulting change in resistance or in calculated dimension is of more moderate degree. At most, structural change in the calibre of efferent vessels would increase the unit efferent resistance by an average of 160 per cent or reduce the radius by 21 per cent. An element of vasoconstriction is indicated to be present in the efferent vessels. Here also the calculated radial constriction is almost as great if not greater in the O group than in the Y group, and thus the calculated resistance due to vasoconstriction is greater in the renal efferent vessels of the old subjects than in the young. Consistent but less marked alterations are derived for the M group of subjects of intermediate age.

It may be speculated that the vasomotor state of the renal circulation of the old subjects studied is not maintained purely for the regulation of blood flow in that organ. Were this so, the afferent vasoconstriction should be completely abolished. The additional resistance which is present, therefore, must be due to the need for extrarenal control of blood flow or must be present because of renal requirements for other than volume flow of blood. The increased efferent constriction likewise cannot be in response to the renal need for blood, but it may serve a renal functional purpose by promoting a greater filtration efficiency.

Summary

From an interpretation of resistance calculations based upon stated assumptions, we have made estimates of the nature and the extent of the changes in the renal circulation of older individuals. It is postulated that removable vasoconstriction not only persists but becomes more manifest in the presence of structural changes.

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Litter Seriation Phenomena in Fibrosarcoma Susceptibility

A Contribution to the Subject of Cancer Susceptibility in Relation to Age

LEONELL C. STRONG

A RELATION between susceptibility to induced fibrosarcomas and litter seriation in mice was discovered incidentally to a genetic analysis of cancer.

The survival time of female mice bearing chemically induced fibrosarcomas with latent periods of less than 100 days gradually increased in litters of older mothers. The survival time increased from 53 days for female mice of first litters to 130 days for female mice of eighth litters (9). The induced fibrosarcomas invaded into the abdomen (invasiveness) less frequently in mice of both sexes in successive litters (10). Finally a sex differential in relation to the percentage of mice developing fibrosarcomas with latent periods of less than 100 days gradually increased in mice of successive litters (11).

In this paper a resumé is given of the results already published on litter seriation together with new data bearing upon the same problem. The characteristics of (a) the latent period, (b) the survival time, (c) the age of death, (d) the sex differential, and (e) the invasiveness of the tumors are presented separately. Whenever practical, the analysis of the data is given without regard to litter seriation and by taking litter sequence into consideration.

MATERIALS AND METHODS

Mice of 4 genetically related strains were used in this experiment (Pedigree 1). The origins of 2 of these groups of mice (the Prunt and the 2Prunt) have been discussed previously (9, 10, 11). The other 2 groups (the Pridil and the IpBr) were produced by outcrosses of 2Prunt mice to mice of the Strong I strain (12).

The pBr strain was 1 of the 4 original sublines of the NHO strain. Mice of this strain were injected with methylcholanthrene since the F_3 generation. The pBr mice possessed the genetic mutants pink eye, brown, and nonagouti (genetic formula ppbbaa). The direct descent of pBr mice (both parents in each generation) have been injected with methylcholanthrene for 25 generations (F_3-F_{27}). A continuous genetic selection toward a greater resistance to all chemically induced tumors has been practised (13).

The average latent period for the appearance of chemically induced tumors in the original pBr mice of the F_{10} generation was 125 days. Genetic selection has increased this latent period to a maximal value of 136 days in mice of the F_{25} generation. In the F_{17} generation the average latent period for chemically induced tumors was 363 days and in the F_{20} generation this average was 393 days. From the F_{17} generation and from the F_{20} generation mice were continued as untreated descents, hence the origin of the Prunt subline from the F_{17} generation and the 2Prunt subline from the F_{20} generation. Each subline has been continued to the F_{30} generation. Thus mice of the 2 sublines should be genetically related by common descent for 17 generations and any biologic differences may then be due either to newly appearing mutations since their separation or a residuum of genetic heterozygosity which must be of slight effect after 17 generations of inbreeding.

In the F_{25} generation a female of the 2Prunt

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descent was outcrossed to a male of the F_{43} generation of the I stock. The F_2 population of this cross consisted of 4 genetic classes: pink-eye, brown; pink-eye, brown, piebald; pink-eye, dilute, brown; and pink-eye, dilute, brown, piebald. The pink-eye dilute brown segregates were continued by sib matings for 10 generations as the Pridil subline. A male mouse of the 2Prunt descent (F_{20}, 46,097 ♂) was outcrossed to a female mouse of the I strain (F_{43}, 46,080 ♀) and the ensuing pink-eye dilute brown segregates of the F_2 generation have also been continued for 10 generation (the IpBr descent). In this paper the Pridil and IpBr observations are used only as further evidence bearing upon sex linked inheritance of susceptibility to chemically induced fibrosarcomas or on maternal inheritance for the same type of tumor.

At 60 days of age all mice received subcutaneously into the right side 1 mg. of methylcholanthrene dissolved in 0.1 cc. sesame oil. In this experiment only the progeny of mice received methylcholanthrene—not the parents. Very few mice had tumors within less than sixty days. Beginning at sixty days following the injection of methylcholanthrene all mice were observed for tumors at the site of the injection of methylcholanthrene. When nodules became firm and increased progressively in size with time, the estimation of the latent period was made. The latent period was taken to be the time between the injection of the methylcholanthrene and the time of first appearance of progressive increase of size of firm nodules. The mice were permitted to live until spontaneous death. The time between the appearance of the tumor and death was taken to be the survival time. Thus the latent period plus the survival time plus the 60 days at which all mice were injected with methylcholanthrene would be the age at death. Since, however, the injection of methylcholanthrene at 60 days of age is constant for all classes, it has been decided for statistical analysis to consider that latent period plus survival time is a measure of age of death due to the presence of a chemically induced fibrosarcoma.

In this paper only the mice dying with a chemically induced fibrosarcoma are considered. These mice bore tumors of all sizes. The presence of the tumor contributed to the death of the animal but may not have been the exclusive cause.

Some mice were excluded from the present analysis. These included all mice dying without tumors, mice with tumors at sites other than the point of the injection of methylcholanthrene (right side of the body), all mice showing ulcerating tumors, mice in which tumors regressed, and mice developing tumors other than fibrosarcomas.

At death the tumor was measured and an autopsy performed. All lesions were preserved in Bouin's solution and stained with hematoxylin and eosin.

The statistical analysis of the data is based upon either χ^2 or the median and probable error where

$$\text{P.E.} = \frac{\text{average quartile deviation from median.}}{\sqrt{N}}$$

Where convergence or divergence was to be measured, the determination of trends by slope was used and the two slopes compared directly or to slope "o". For presentation of data in curve form, the three-point moving average for smoothing frequency distributions was also used.

Results

To date, 1309 mice of the 4 series (Prunt, 2Prunt, Pridil, and IpBr) have died with chemically induced fibrosarcomas. Of these 445 belonged to the Prunt, 604 to the 2Prunt, 143 to the Pridil, and 117 to the IpBr descent (table 1). These mice belonged to the first to the twelfth litters, although the numbers belonging to the advanced litters were small. A few mice with latent periods of more than 400 days for chemically induced fibrosarcomas were also not included in table 1.

Observations Without Relation To Litter Seriation

Female mice of the Prunt descent had their tumors earlier than did the males (fig. 1). The difference between the medians for the sexes is 37 days ± 3.63, or more than 10 times the P.E., which is statistically significant.

Male mice of the Prunt descent had shorter survival time values than did the females (fig. 2). The difference between the medians of the sexes is 29 days ± 2.86, or more than 10 times the P.E., which is significant.

Table 1. Distribution of Tumors (Sexes Separate) for the 4 Groups of Mice Used. Mice Divided into 4 Classes Based Upon the Latent Periods for the Appearance of Tumors.

Average L. P.	Latent Period															
	— 100				101–200				201–300				301–400			
	♀	♂	%♀	%♂	♀	♂	%♀	%♂	♀	♂	%♀	%♂	♀	♂	%♀	%♂
2 Prunt	119	41	74.4	25.6	189	162	53.8	46.2	26	49	34.7	65.3	6	12	33.3	66.7
Prunt	84	25	77.1	22.9	148	124	54.4	45.6	16	36	30.8	69.2	4	8	33.3	66.7
Pridil	22	2	91.7	8.3	61	30	67.0	33.0	7	17	29.2	70.8	2	2	50.0	50.0
IpBr	31	16	66.0	34.0	13	18	41.9	58.1	9	5	64.3	35.7	9	16	36.0	64.0
Total	256	84	75.3	24.7	411	334	55.2	44.8	58	107	35.2	64.8	21	38	35.6	64.4

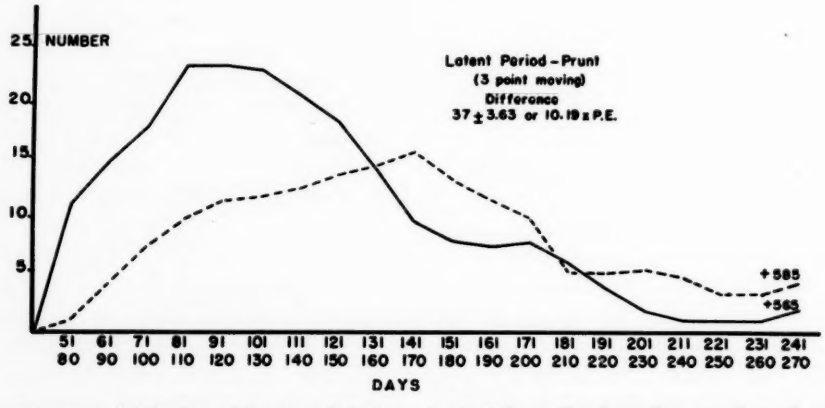

Fig. 1. Frequency distribution of latent periods for fibrosarcomas in female mice (solid line) and male mice (short dash line) for Prunt mice. Time in days is plotted on the base line, number of mice with tumors on the vertical line (3-point moving system).

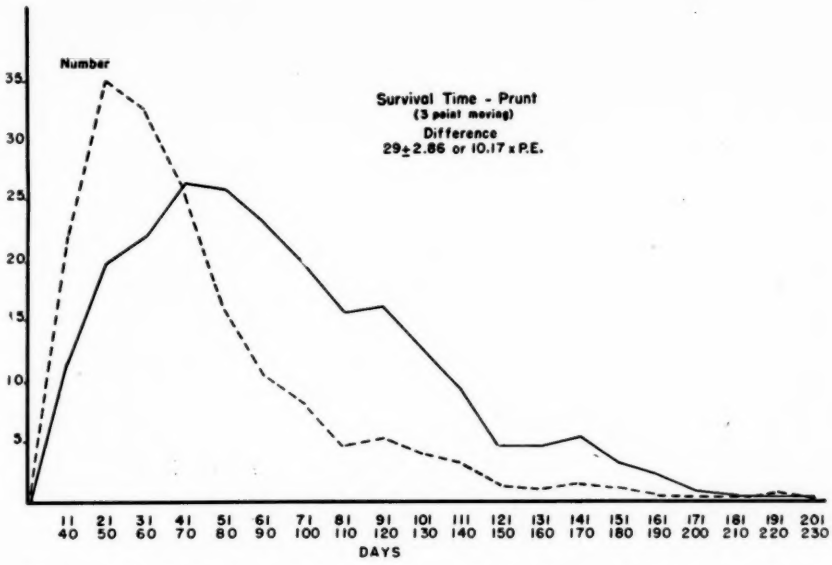

FIG. 2. Frequency distribution of survival time for Prunt mice bearing fibrosarcomas; females on solid line, males on short dash line. Time in days plotted on the base line, number of mice on the vertical line (3-point moving system).

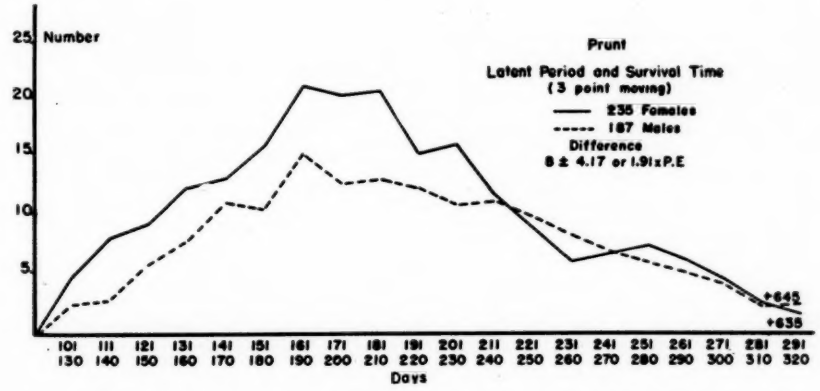

FIG. 3. Data for charts 1 and 2 added together giving age of death for Prunt mice; female mice on solid line, males on short dash line. Time in days plotted on the base line, number of mice on the vertical line (3-point moving system).

Figure 3 gives the data of fig. 1 and 2 (latent period plus survival time = age of death) added together. Here the difference between the sexes for Prunt mice is not significant (8 days ± 4.17 or 1.91 times the P.E.). Thus one sex difference appears to neutralize the other sex difference.

Female mice of the 2Prunt were more susceptible than males (fig. 4). The difference between the medians of the sexes is 40 days

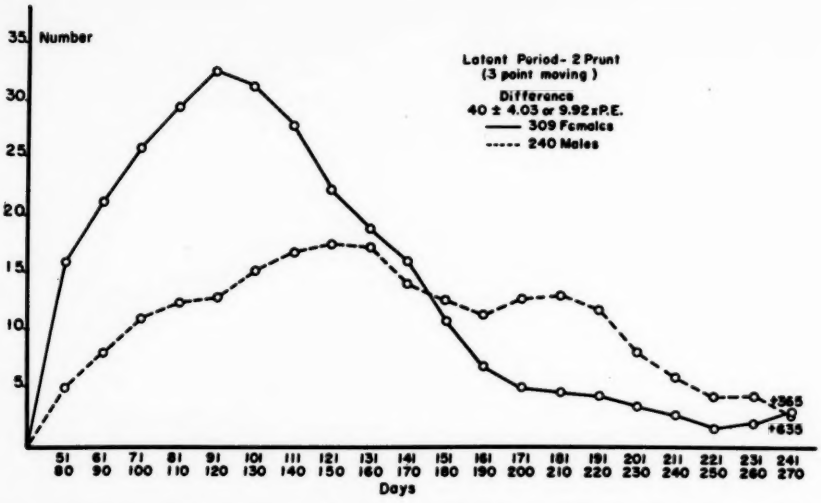

FIG. 4. Latent period for fibrosarcomas in mice of 2 Prunt descent; females on circle and solid line, males on circle and short dash line. Time in days is plotted on the base line, number of mice on the vertical line (3-point moving system).

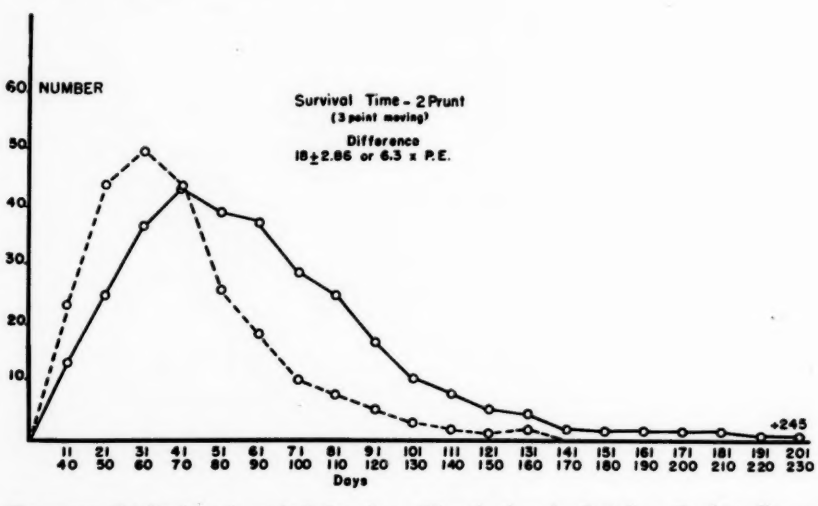

FIG. 5. Frequency distribution of survival time for 2 Prunt mice bearing fibrosarcomas; females on circle and solid line, males on circle and short dash line. Time in days is plotted on the base line, number of mice on the vertical line (3-point moving system).

± 4.03 or 9.92 times the P.E., which is significant.

Male mice of the 2Prunt descent showed lower survival time values, on the average, than did the females (fig. 5). The sex difference of the medians is 18 days ± 2.86 or 6.3 times the P.E. This sex difference is significant.

Figure 6 combines the data of figs. 4 and 5, that is, latent period and survival time are added together. There is a sex difference of the

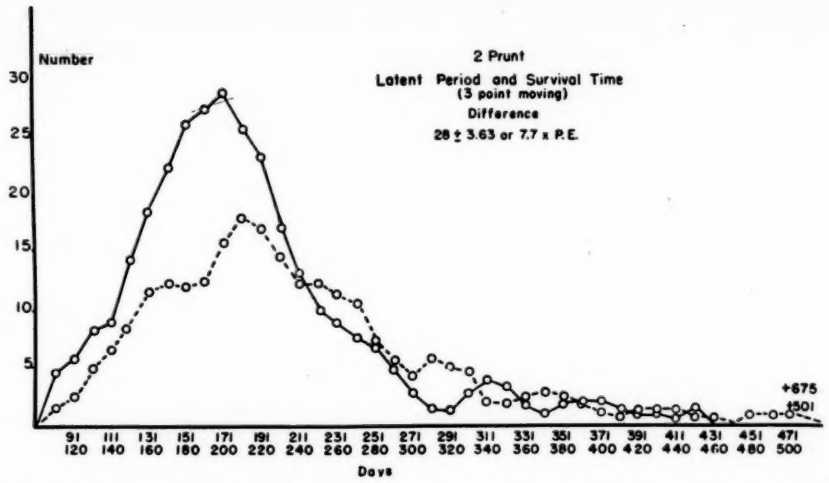

FIG. 6. Data for charts 4 and 5 added together = age at death of 2Prunt mice bearing fibrosarcomas; female mice with circle and solid line, males with circle and short dash line. Time in days is plotted on the base line, number of mice on the vertical line (3-point moving system).

medians in age of death for 2Prunt mice of 28 days ± 3.63 or 7.7 times the P.E. This difference is significant.

The analysis of the data of figures 1 to 6 indicates that two mechanisms are involved. Sex is involved in each mechanism. One of these mechanisms determines the latent period at which a chemically induced fibrosarcoma appears and the other mechanism determines, in part, the survival time or the length of time a mouse will live with a growing fibrosarcoma. These two mechanisms are partially complementary or reciprocally related to each other, one neutralizing the effect of the other in the Prunt descent, but not completely so in the 2Prunt descent since there is still a significant difference between the sexes in the age of death (latent period plus survival time) for mice of this descent (28 days ± 3.63 or 7.7 times the P.E. (fig. 6).

Figure 7 shows the same data as given in figures 1 to 6. The data are given by the quartile method with time expressed in days given on the base line. Data for the Prunt descent are given on the top line, for 2Prunt on the second line, and thus alternately for all the classes. The 3 sets of data on Latent Period (L.P.), Survival Time (S.T.), and Age of Death (D) are separately given. The number of determinations is given and the total number of observations, 2799, indicated (3 determinations on 933 mice growing chemically induced fibrosarcomas). There is apparently a significant difference between the 2 groups of females for survival time, which amounts to 9.0 days ± 2.72 or 3.3 times the P.E. This difference is reflected into the data for the age of death where the difference is 19.0 days ± 3.5 or 5.42 times the P.E. The P.E. are given and the sex differences again indicated, which give significant differences except in age of death for females and males of the Prunt descent as indicated also in figure 3.

Figure 8 and table 1 give the data on latent period and percentage susceptibility for the 4 strains of mice used together with comparable data obtained with I strain mice. The mice are divided into 4 classes based upon latent periods of tumors. Class 1 consists of mice with latent periods less than 100 days; class 2, latent periods between 101 and 200 days; class 3, between 201 and 300 days; and class 4, between 301 and 400 days. The individual points are based upon the percentage of fe-

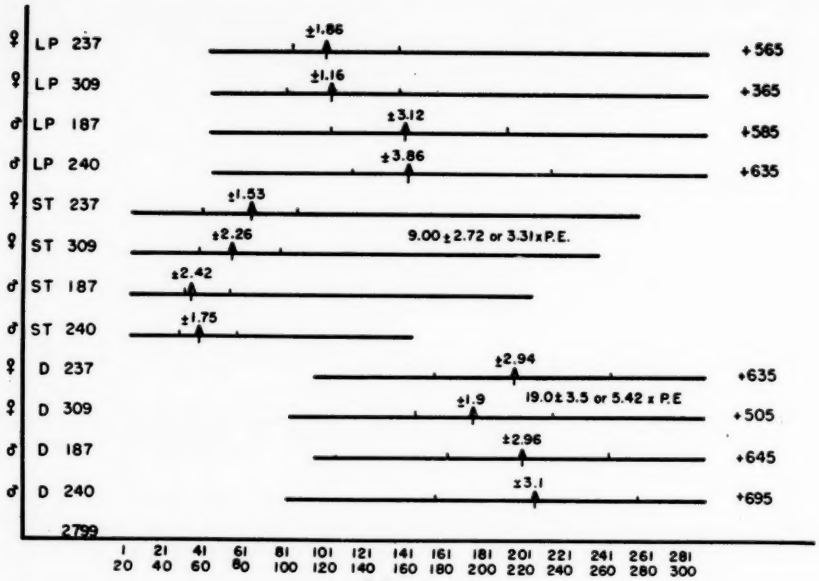

FIG. 7. Data on latent period (L.P.), survival time (S.T.), and age of death (D). The number of determinations are given and the data on the sexes are separate. Probable errors are noted over the medians (arrows). Earliest data are given to the left of the chart, the 25 per cent of data appears first on line, 50 per cent with P.E. over the medians (arrows), and 75 per cent of data on next one-half bar. The latest data are given to the right of line, in some cases expressed in days.

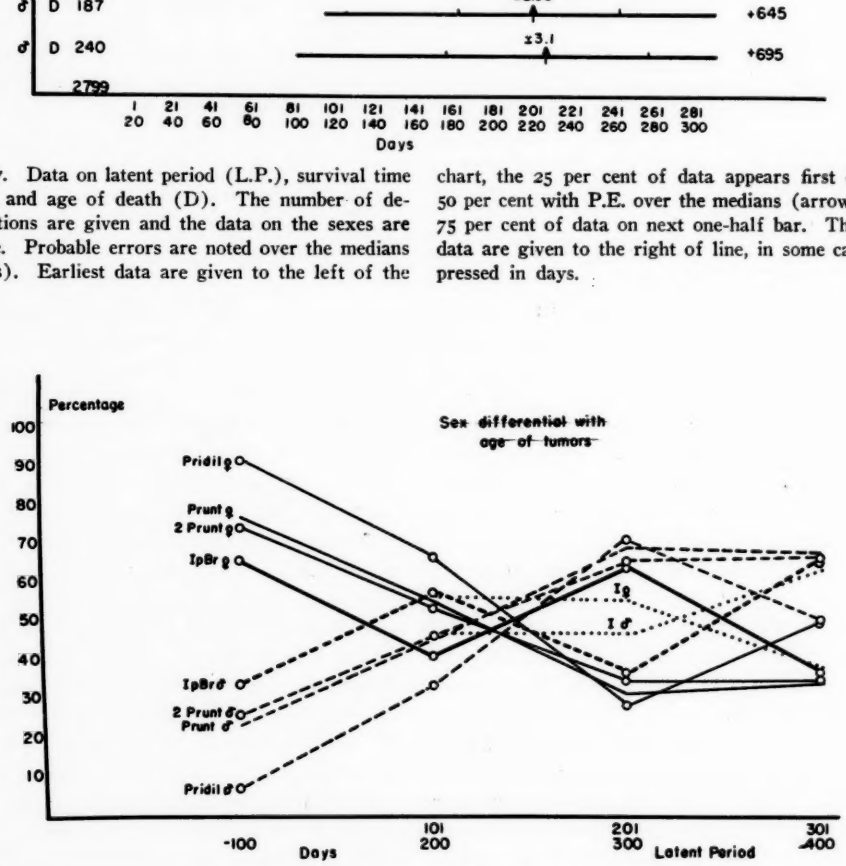

FIG. 8. The percentage of mice developing fibrosarcomas with latent periods of 4 classes for the 4 sublines of mice used. "I" strain mice are also indicated (dotted line). Sexes are given separately.

males with tumors compared with the percentage of males with similar tumors in each age class.

The two sublines, Prunt and 2Prunt, show very similar trends, giving a greater sex differential in class 1 and a small sex differential in the opposite direction in classes 3 and 4. There is no sex differential in mice of the I strain, for any class. The Pridil shows the greatest sex differential in class 1 of all the sublines (91.7 per cent in ♀ ♀ : 8.3 per cent in ♂ ♂) and mice of the IpBr show the least (66.0 per cent in ♀ ♀ : 34.0 per cent in ♂ ♂).

This is evidence that the mechanism involved in the determination of the sex differential in relation to the latent period for the appearance of chemically induced fibrosarcoma is either sex-linked or is determined by maternal inheritance.

Figure 9 presents the data on latent periods for sublines Prunt and 2Prunt in terms of percentage incidence. The data are also given in table 2. The 2 groups of females are quite similar and the 2 groups of males are similar but there is a sex differential, the females developing their tumors earlier than do the males.

Observations Relating to the Effect of Litter Seriation

Up to now litter seriation has been ignored and the data for all litters considered together.

Figure 10 gives the data on the Prunt descent. Litter seriation is plotted along the base line and time in days expressed along the vertical line. The sexes are separated and survival time, latent period, and age of death given separately. The most striking effect of litter seriation is the increased sex differential in the latent period. Female mice develop their tumors earlier and earlier in succeeding litters: 160 days in the first litters to 99 days in the seventh litters (fig. 10; table 2). The males did not deviate in this characteristic in subsequent litters. This progressive sex differential is partially reflected in age of death but here divergence between the sexes is probably not significant.

Figure 11 gives comparable data for the 2Prunt descent. Fluctuations between mice of the successive litters interfere with an adequate statistical analysis, but it seems that the data on age of death probably converge, the overall sex difference being significant as in-

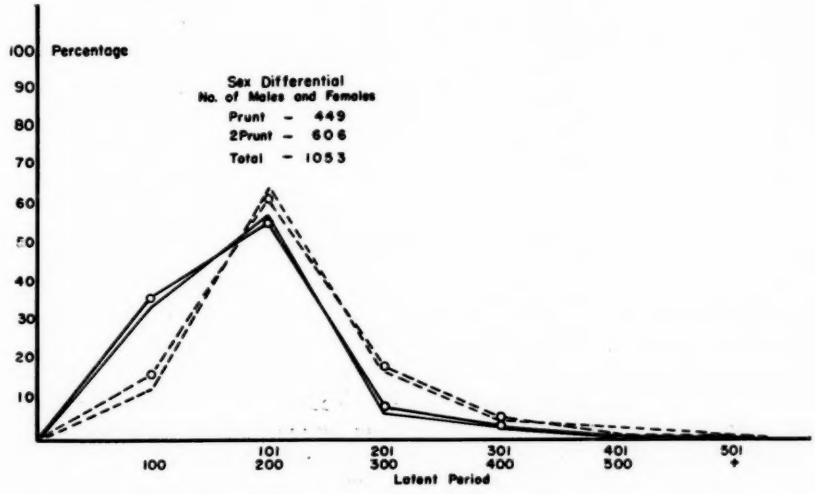

FIG. 9. Percentage incidence of tumors for Prunt and 2Prunt sublines (sexes separated). Latent period is given on base line and percentage of mice showing tumors on the vertical line.

TABLE 2. FREQUENCY DISTRIBUTION OF FIBROSARCOMAS IN 2 SUBLINES, PRUNT AND 2 PRUNT. FIVE CLASSES OF MICE BASED UPON LATENT PERIODS ARE GIVEN. NUMBER OF MICE (SEXES SEPARATED) IS ALSO GIVEN.

Stock		Latent Period									
		— 100		101–200		201–300		301–400		400 +	
		No.	%	No.	%	No.	%	No.	%	No.	%
Prunt											
♀	253	84	33.2	148	58.5	16	6.3	4	1.6	1	0.4
♂	196	25	12.8	124	63.3	36	18.4	8	4.1	3	1.5
Total	449	109	24.3	272	60.6	52	11.6	12	2.7	4	0.2
2 Prunt											
♀	341	119	34.9	189	55.4	26	7.6	6	1.8	1	0.3
♂	265	41	15.5	162	61.1	49	18.4	12	4.5	1	0.4
Total	606	160	26.4	351	57.9	75	12.4	18	3.0	2	0.3

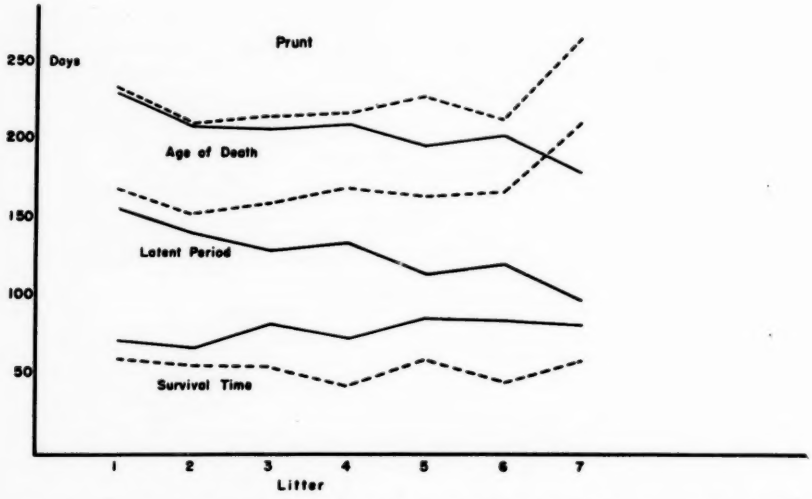

FIG. 10. Prunt mice for (a) age of death, (b) latent period, and (c) survival time; females on solid lines, males on short dash lines. Litter frequency is plotted on the base line; time in days is plotted on the vertical line. (Not based on 3-point moving method).

dicated in figures 6 and 7 with no sex differential in the early litters.

Inspection of figure 10 indicates that a further analysis for latent periods is called for. Figure 12 presents these data. Litter seriation is given on the base line and the percentage of mice developing chemically induced fibrosarcomas with latent periods less than 100 days on the vertical line.

The data for Prunt descent again show divergence between the sexes (females on solid line; data for males on short dash line). These

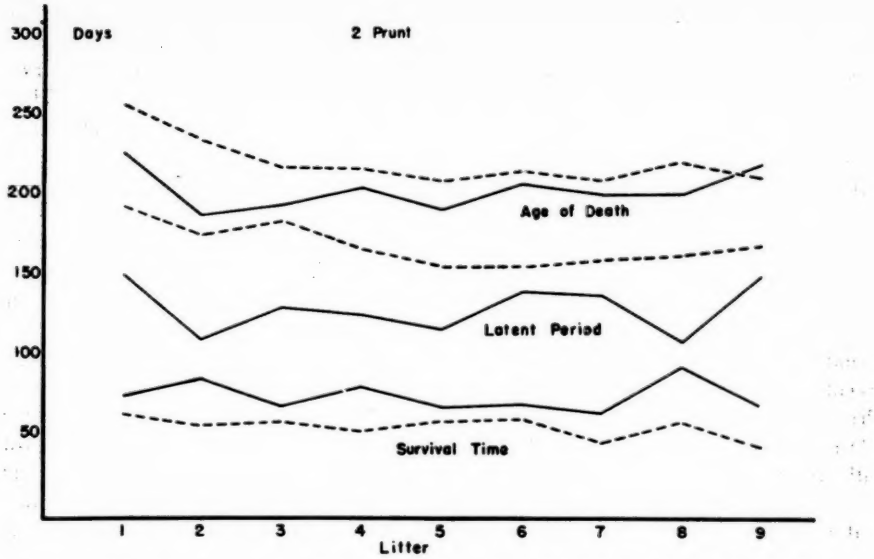

FIG. 11. 2Prunt mice for (a) age of death, (b) latent period and (c) survival time; females on solid lines, males on short dash lines. Litter seriation is plotted on the base line; time in days is given on the vertical line. (Not 3-point moving system).

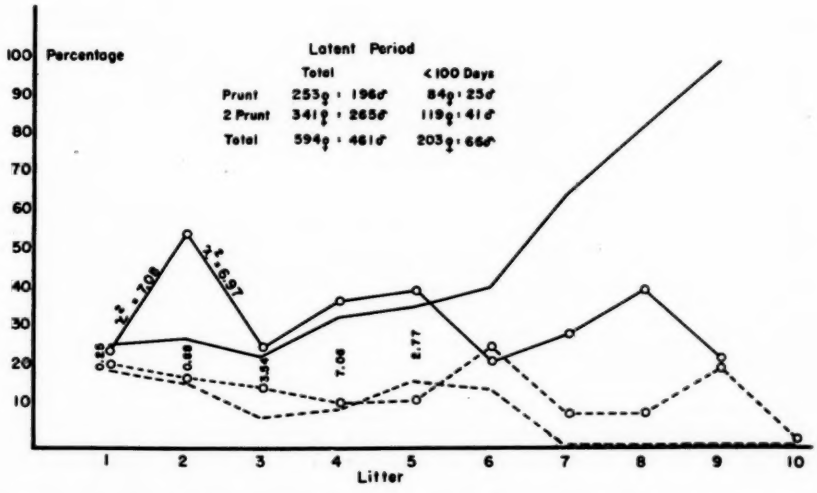

FIG. 12. Litter frequency is given on the base line and percentage frequency of mice developing fibrosarcomas with latent periods of less than 100 days on the vertical line. Females of Prunt descent are given on solid line, males of same strain on short dash line. Females of 2Prunt descent are shown on circle and solid line, males for 2Prunt descent on circle and short dash line. The χ^2 differences of individual points of the curves are given at significant places.

data show a converse relationship to data of figure 10. In each case it is the female that changes with litter seriation. As the latent period diminishes with litter seriation in females, the percentage of females that develop tumors with latent periods less than 100 days increases. The χ^2 determinations of sex differences for the first 5 litters are as follows: litter 1, 0.25; litter 2, 0.88; litter 3, 3.54; litter 4, 7.06; and litter 5, 2.77. The number of mice for litters 6, 7, 8, 9, and 10 are too small for χ^2 determinations but the probable trends are indicated. Figure 12 also gives the 2Prunt descent. The data for the 2 groups of males (Prunt and 2Prunt) are quite similar. Female mice of the second litters deviate significantly from female mice of the first litter ($\chi^2 = 7.08$) and also from female mice of the third litters ($\chi^2 = 6.97$). Female and male mice of the 2 groups for the third, fourth, and fifth litters are quite similar.

Figure 13 and table 3 give Survival Time for mice of the Prunt descent. The mice are divided into 3 groups depending upon the age at which fibrosarcoma developed: group 1, latent periods less than 100 days; group 2, latent periods between 101 and 200 days; and group 3, latent periods between 201 and 300 days. The data for females are given on the solid lines and for males on the short dash line. The data are combined for mice of litters 1 to 4, mice of litters 5 to 8, and mice of litters 9 to 12. Females show more variability between litters when tumors develop early and late than they do in mice with latent periods between 101 to 200 days. There is a pronounced sex differential and the females seem to be more variable than do males. The

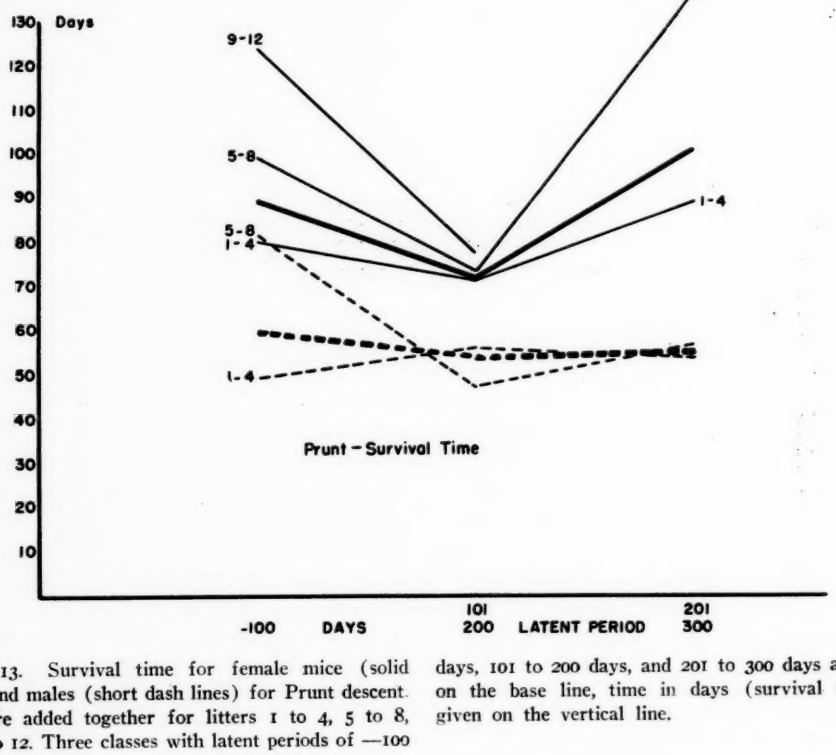

FIG. 13. Survival time for female mice (solid lines) and males (short dash lines) for Prunt descent. Data are added together for litters 1 to 4, 5 to 8, and 9 to 12. Three classes with latent periods of —100 days, 101 to 200 days, and 201 to 300 days are given on the base line, time in days (survival time) is given on the vertical line.

TABLE 3. SURVIVAL TIME FOR MICE BEARING FIBROSARCOMAS IS GIVEN. LITTERS 1 TO 4, 5 TO 8, AND 9 TO 12 ARE ADDED TOGETHER. NUMBER OF MICE AND AVERAGE SURVIVAL TIMES ARE ALSO GIVEN.

Stock and Litters	Latent Period					
	— 100		101–200		201–300	
	No.	S. T.	No.	S. T.	No.	S. T.
Prunt						
1–4 ♀	46	80.5	96	72.2	12	89.6
5–8 ♀	36	99.5	47	72.1	4	137.3
9–12 ♀	3	124.0	5	77.2		
Total	85	90.1	148	72.4	16	101.5
1–4 ♂	17	50.0	84	55.8	23	55.5
5–8 ♂	8	81.8	37	48.9	13	56.8
9–12 ♂			3	76.7		
Total	25	60.2	124	54.2	36	55.9
2 Prunt						
1–4 ♀	77	78.3	116	71.7	21	84.7
5–8 ♀	41	73.9	72	70.0	4	81.0
9–12 ♀	3	60.3	5	65.8	1	103.0
Total	121	76.3	193	70.9	26	84.8
1–4 ♂	26	61.4	91	54.6	33	60.1
5–8 ♂	15	49.4	72	53.2	14	53.3
9–12 ♂	1	47.0	2	42.0	2	40.0
Total	42	56.8	165	53.8	49	52.3

sequence of survival time value for females of early appearing tumors is litters 1 to 4, 5 to 8, and 9 to 12 (there are no data of litters 9 to 12 with latent periods of tumors between 201 to 300 days).

Figure 14 and table 3 show survival time values for mice of the 2Prunt descent. There is a pronounced sex differential in survival time values and in females; at least there seems to be more variation in early and late-appearing tumors than in the class which developed tumors between 101 to 200 days.

The sequence of survival time value for female mice of the 2Prunt descent with latent periods of less than 100 days is litters 9 to 12, and 1 to 4, the reverse for female mice of the Prunt descent.

Figure 15 compares the data for female mice of litters 5 to 8 for Prunt and 2Prunt sublines. The survival time values for female mice with tumors of latent periods between 101 to 200 days are the same for the 2 sublines of females, whereas with early appearing tumors there is a significant difference between the 2 groups, as indicated by figure 16. The difference in survival time values for female mice with latent periods of less than 100 days was 21.0 days $\pm$ 5.7 or 3.68 $\times$ P.E. The data for litter 9 to 12 are still too small for further statistical analysis.

Figure 17 and table 4 give the data on invasiveness for the 2 groups of Prunt and 2Prunt descents. In both series the data for litters 1 to 2, 3 to 4, 5 to 6, 7 to 8, and 9 to 10 are added together. There is again a significant sex differential, the females showing more tumors that invade into the abdomen than do males. The χ^2 for sex differential for Prunt descent is 4.38; for 2Prunt descent, 5.00; and for combined Prunt and 2Prunt, 9.24. All these values are statistically significant.

The trend of all curves seems to be downward for litter seriation, except for female mice of the Prunt descent, but even here the curve reaches 0 value for invasiveness at litters 7 to 8. For χ^2 determinations on trends the data for litters 1 to 6 are combined and compared for litters 7 to 12. This classification was arbitrarily chosen. The χ^2 for Prunt data on litter seriation could not be used since the class on invasive tumors in litters 7 to 12 was zero. The χ^2 for 2Prunt descent is 3.11 and for combined Prunt and 2Prunt, 6.40. Both of these values indicate a significant decline in occurrence of invasive tumors in mice of succeeding litters.

DISCUSSION

The use of inbred mice has made possible many contributions in cancer research. Much

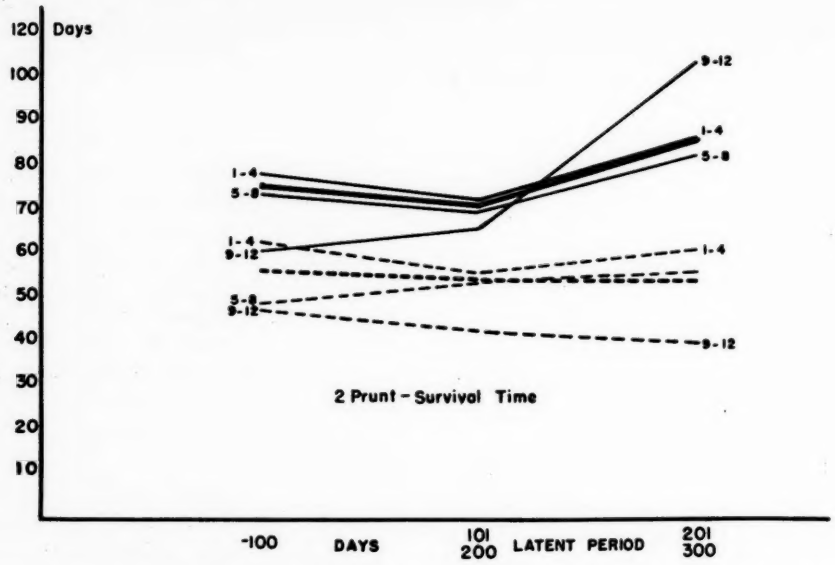

FIG. 14. Survival time for female mice (solid lines) and males (short dash lines) for 2Prunt descent. Data are added together for litters 1 to 4, 5 to 8, and 9 to 12. Three classes with latent periods —100 days, 101 to 200 days, and 201 to 300 days are plotted on the base line, time in days (survival time) is given on the vertical line.

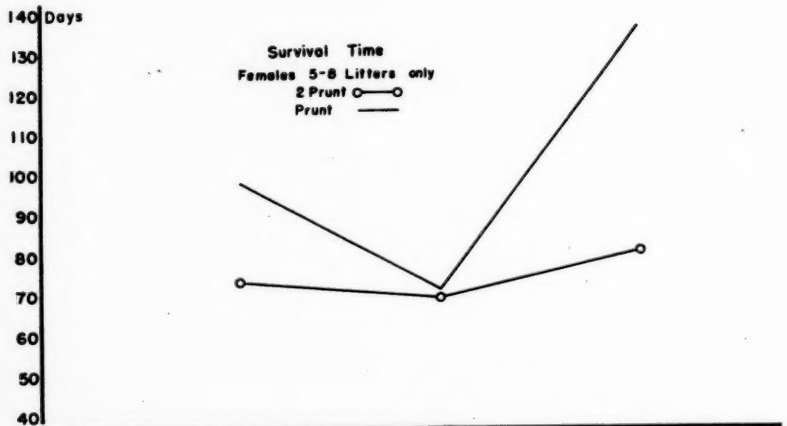

FIG. 15. Survival time for female mice of Prunt descent (solid line) compared to data for female mice 2Prunt descent (circle and solid line). Data for litters 5 to 8 are added together. Latent period is plotted on base line. Survival time in days is given on the vertical line.

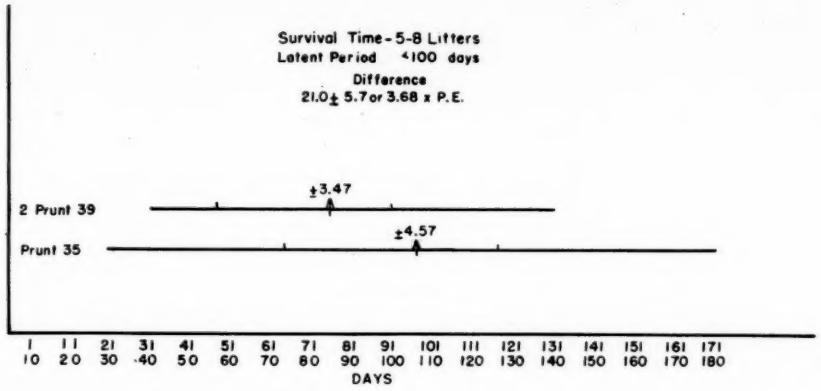

FIG. 16. Survival times for females of 5 to 8 litters compared. Analysis is by average quartile method. Time in days is plotted on the base line.

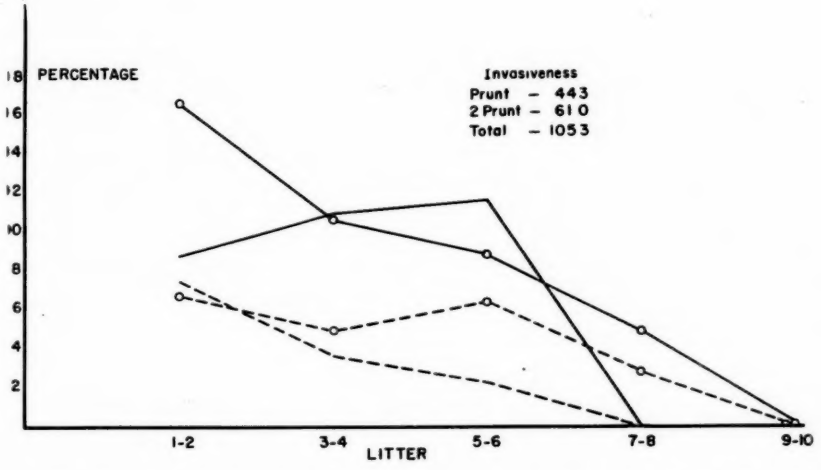

FIG. 17. Invasiveness of fibrosarcomas are plotted. Litter frequency is given on the base line, percentage of mice with invasive tumors on the vertical line. Prunt females are shown on solid line, Prunt males on short dash line, 2Prunt females on circle and solid line, 2Prunt males on circle and short dash line.

is now known of the genetic nature of susceptibilities to spontaneous, transplanted, and chemically induced tumors in mice. This conclusion applies especially to adenomas of the lung and to adenocarcinomas of the mammary gland. Bittner (1) has proposed a simple formula for spontaneous breast tumors consisting of influences, as follows: genetic, milk inciter, and hormonal. In addition to these influences on this particular neoplasm there have been disclosed a dietary influence (such as caloric restriction, and high fat diet) and the complex biologic influences initiated by forced breeding where the final effect may be something more than the normal hormonal relationships within the body. The analysis of the data bearing upon cancer susceptibility indicates that the entire mechanism has not been com-

TABLE 4. INVASIVENESS OF TUMORS FOR THE TWO SUBLINES PRUNT AND 2 PRUNT.

Stock	Litters	Local Only	Invasion	Total	x^2 Determinations
Prunt ♀	1–12	226	23	249	
♂	1–12	186	8	194	
Total	1–12	412	31	443	$x^2=4.38$
2 Prunt ♀	1–10	304	36	340	
♂	1–10	255	15	270	
Total	1–10	559	51	610	$x^2=5.00$
Prunt ♀ + 2 Prunt ♂	1–12	530	59	589	
	1–12	441	23	464	
Total	1–12	971	82	1053	$x^2=9.24$
Prunt ♀+♂	1–6	366	31	397	
♀+♂	7–12	46	0	46	
Total	1–12	412	31	443	
2 Prunt ♀+♂	1–6	475	48	523	
♀+♂	7–10	84	3	87	
Total	1–10	559	51	610	$x^2=3.11$
Prunt ♀+♂ + 2 Prunt ♀+♂	1–6	841	79	920	
	7–12	130	3	133	
Total	1–12	971	82	1053	$x^2=6.40$

pletely disclosed. There is a concept that this deficiency may be supplied by the idea of somatic mutation, even though the evidence for a somatic mutation in the origin of cancer must always be of an indirect nature.

The present experiment on litter seriation indicates that there are inherited factors in cancer susceptibility (latent period) and certain attributes of malignancy (survival time and invasiveness) that cannot be completely controlled by the accepted method of inbreeding (brother-to-sister matings to produce an inbred or homozygous strain). These characteristics of cancer (susceptibility and attributes of malignancy) are influenced by some subtle mechanism which changes during the lifetime of the mother and is selectively handed down to her progeny in successive litters by some mechanism other than through the chromosomes or genes.

This new concept has nothing to do with the theory of somatic mutations in the origin of cancer.

The phenomenon of litter seriation or of the age of the mother influencing biologic characteristics of her progeny is not unique in the literature. A few illustrations only will be mentioned here.

Ingle and associates (3) concluded that in Daphnia "longevity seems to be independent of total numbers of young produced, but there are indications of a relationship existing between longevity and age at greatest reproductive activity."

Lansing (5, 6) found that the mean life span of the rotifers *Philodina citrina* and *Euchlanis triquetra* is shorter for offspring born later in the mother's life than those born earlier. The older the orthoclone, the shorter is the number of generations until complete extinction of the line occurs. One suggestion has been made that the eggs are laid with an increasingly greater accummulation of an aging factor as the mothers age, so that the younger eggs are off to a better start. Edmondson (2) in a discussion of Lansing's work agrees that any explanation for the effect of mother's age on longevity of her offspring "must account for the cumulative and reversible features as well as the apparent transmission through the egg cytoplasm, and the effectiveness of calcium in the culture medium."

In 1941 Penrose (7) arrived at the conclusion that "the most important factor in the origin of the 'mongol' type of imbecile is associated with the age of the mother at the time of pregnancy. The affected child is often the last born in a large family, but the cause is not dependent upon maternal exhaustion

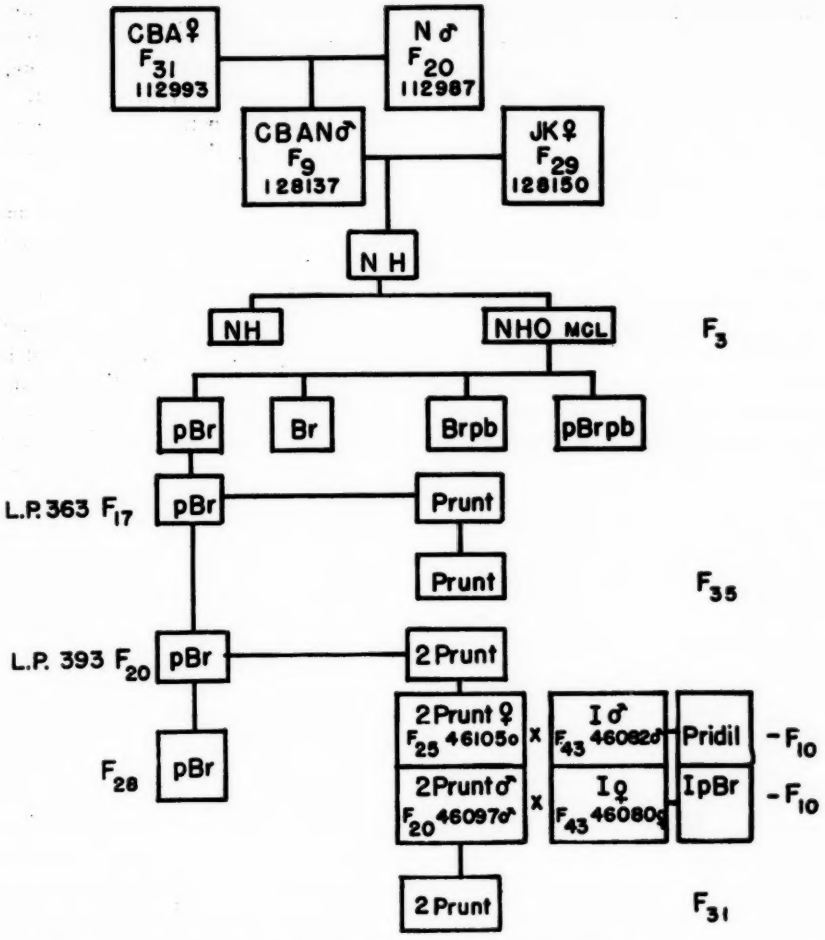

FIG. 18. Pedigree 1: The genetic relationship between 4 sublines of the NH strain. These are Prunt, 2Prunt, Pridil, and IpBr. L.P. = latent period for fibrosarcomas, MCL = Methylcholanthrene.

through too frequent child bearing—it depends upon maternal age alone. The risk of a woman's giving birth to a 'mongol' child is approximately doubled every five years after she reaches the age of 25. The father's age does not seem to matter at all. There are also other abnormalities of development of the nervous system in which cause is associated with the age of the mother."

Bittner (1) has reported an increased incidence of mammary gland tumors in advanced litters of mice and explains the phenomenon in terms of the milk inciter. He states, "These results indicated that the milk agent was not transferred to the mice born in the early litters, but was obtained by offspring born to the same mothers in the succeeding litters." These data however may now be interpreted in terms of litter seriation where the effect on the offspring may be due to a similar mechanism (cytoplasmic ?) which is indicated for chemically induced fibrosarcomas.

MacDowell and his associates (4) have reported a decrease in the incidence of leukemia in succeeding litters of mice born to the same parents. They conclude, "Mother's age has an outstanding influence on the incidence of spontaneous leukemia in hybrid mice. Mice from younger mothers showed a distribution of leukemia markedly higher than that for mice from the older mothers. A more complete analysis of the data shows a progressive reduction in the proportion of leukemia as mother's age increases." And further: "It is possible that the influence of a female as a mother and as a nurse is dependent on the same mechanism but if so why should the effect from mothers increase with age and the effect from nurses disappear? The increasing divergence with age of mice from mothers of different strains more closely parallels the expression of sex difference and suggests that the maternal influence is intrinsic or germinal."

The present experiment, showing relationship between cancer susceptibility and litter seriation (mother's age ?), also may have a bearing upon the problem of tissue specificity. The transplantation of neoplastic tissue has disclosed that the specific reaction of a mouse towards a transplant is reached only during early sexual life (8). This characteristic of the individual is gradually attained during adolescence and is again gradually lost during senescence. Litter seriation is apparently exerting a comparable influence on chemically induced fibrosarcomas. However, the present data do not include observations during adolescence and senescence of mothers but only on female mice during early and middle sexual life. Trends in these age groups however are statistically significant.

Mice of the Prunt and the 2Prunt strains are genetically very similar. They have had 17 generations of inbreeding in common. They differ, however, in relation to the characteristics of chemically induced fibrosarcomas associated with litter seriation (susceptibility or latent period, and malignant features or survival time and invasiveness). These differences may be due to the fact that the mice reach maximal sexual activity in relation to the production of young at different chronologic times so that the progeny of the sixth litter of one strain may be comparable to mice of the seventh litter of the other strain or to some other similar relationship.

Further analysis may eventually bring the data on litter seriation more into harmony with genetic determination or resolve itself into "cytoplasmic" inheritance. For the present, however, further hybridization upon which a genetic analysis must be based is not indicated —the shift with litter seriation of susceptibility to the chemically induced fibrosarcoma must first be stabilized and this can be done by continuing selective sublines descended from mice of different litters of the same parents.

Summary

A total of 1309 mice of four inbred descents, Prunt, 2Prunt, Pridil, and IpBr have (a) been injected with 1 mg. of methylcholanthrene dissolved in 0.1 cc. of sesame oil at 60 days of age, (b) developed fibrosarcomas at the site of injection, and (c) died. The mice belonged to the 1 to 12 litters. The characteristics of (1) latent period for the appearance of tumors, (2) survival time with the growth of tumors, (3) age of death, (4) a sex differential, and (5) invasiveness or ability to invade into the abdomen are analyzed in terms of litter seriation. A brief review of the literature is given and the problem of tissue specificity is cited.

Mice in successive litters show differences in susceptibility to chemically induced fibrosarcomas (latent period) and in characteristics of malignancy (survival time and invasiveness). There seems to be an inverse relation between survival time and latent period, although two mechanisms appear to be evident. In the Prunt strain female mice develop tumors earlier in succeeding litters, even though the males do not do so, thus bringing about a sex differential in relation to fibrosarcomas which increases in successive litters. Female mice show more tumors with the ability to invade

into the abdomen than do males. The number of mice with malignant tumors (invasiveness) is reduced in mice of both sexes in successive litters. Survival time is also influenced by litter seriation.

The present data indicate two hereditary mechanisms involved in cancer susceptibility and malignancy which change during the life span of a female mouse, and are handed down to her progeny. This transmission is apparently not by way of the chromosomes or genes but may involve cytoplasmic inheritance.

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Studies in Experimental Atherosclerosis

IV. Theoretic and Practical Implications of the Results of Intravascular Injections of Cholesterol Sols

OTAKAR J. POLLAK AND BELLA WADLER

Ever since the rabbit was introduced as an experimental animal for the production of atherosclerosis, the objection was raised that cholesterol is not a normal constituent of the diet of a herbivorous animal. By direct introduction of cholesterol into the circulating blood the digestive system is bypassed. One must not overlook that the architecture of the rabbit's blood vessels is not exactly the same as that of man; experimental results valid for the rabbit need not be valid for man.

Atherosclerosis induced in rabbits by feeding of cholesterol differs from the human disease inasmuch as it is necessary to render the rabbit hypercholesteremic. Rarely are atherosclerotic lesions found in a rabbit unless its blood cholesterol reaches the level of 450, 650, or 800 mg. per 100 ml. In the few instances where vascular alterations are found in rabbits with a less severe hypercholesteremia the elevation of blood cholesterol was, as a rule, of long duration. In human beings, a normal or only slightly elevated cholesterol level is found even in fully developed atherosclerosis. The disease is not significantly more frequent among patients with diseases associated with hypercholesteremia, such as in patients with diabetes mellitus, lipid nephrosis, myxedema, or familial hypercholesteremia.

Only a few investigators reported vascular alterations after intravascular administration of colloidal cholesterol suspension (for bibliography, see article III of this series. J. Gerontol., 6: 217-228). They introduced sufficiently large quantities of cholesterol to produce a degree of hypercholesteremia comparable to that obtained after prolonged feeding of cholesterol to animals. We succeeded in producing vascular alterations by intravascular injections of material insufficient to elevate the blood cholesterol level of experimental animals. Thus, we created conditions in the rabbit nearer to those observed in human beings suffering from atherosclerosis.

Because of the insignificant blood cholesterol rise in humans with atherosclerosis, the theory has been advanced that the molecular state of the cholesterol is significant rather than its amount. Hueper (10) supported this theory by multiple experiments. He succeeded in inducing atheromatous lesions in dogs, rabbits, and rats by multiple injections of large doses of such macromolecular substances as gelatin, ovalbumin, polyvinylalcohol, methyl cellulose, pectin, and gum acacia. Harrison (7) observed vascular pulmonary lesions in rabbits injected with small particles of fibrin.

Moreton (14) examined blood of individuals nephelometrically during the period of postprandial hyperlipemia. In blood samples taken at intervals after a cream-test-meal the number of fat particles, the so-called chylomicrons, was increased. Elevation of blood cholesterol after meals is not sufficiently high to be detectable by chemical quantitative methods. Moreton (14) believed that chylomicrons contain cholesterol which, in his opinion, is either part of the dietary fat or, as in the case of ingestion of vegetable oils, of biliary origin.

Christianson (3) injected human fat, fatty acids, soaps, and cholesterol directly into the media and subintima of arteries of dogs. He noticed that cholesterol alone was not resorbed. Hirsch (8) injected a similar mixture, namely fat with added cholesterol, into the vascular lumen. The material traversed the vessel wall but for the cholesterol, which was deposited in the arterial wall. Hirsch explained the re-

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Mrs. Bella Wadler received a M.S. degree in chemical engineering from the Institute of Technology, Prague, Czechoslovakia, in 1939. For many years she has been associate in biochemical research at Tufts Medical School in Boston. At present, she is collaborating with Dr. Pollak at the Quincy City Hospital.

tention of cholesterol by pointing out its insolubility. Successful induction of atherosclerosis in rabbits by repeated intravenous injection of staphylococci led Saltykow (19) to believe that atherosclerosis is an inflammatory process. The results of our own experiments, namely, the observation that the larger the size of colloidal particles introduced into the blood stream the smaller the minimum effective dose of cholesterol, are in accord with the "molecular" or "colloidal" theory of development of atherosclerosis.

This does not mean that atherosclerosis is always and solely the result of the presence of large micels in the blood. Experimental atherosclerosis can be produced by various methods, especially by prolonged feeding of cholesterol to animals which results in marked hypercholesteremia. Already in 1905, Wuttig (21) mentioned that in high grade lipemia the chylomicrons tend to form large fat drops. Similarly, the larger the total amount of cholesterol the more likely aggregation into large micels will occur.

It is entirely possible that the effect which is commonly ascribed to the quantitative increase in blood cholesterol is in reality due to its qualitative state, that is, caused by the dyscholesteremia which in such a case accompanies the hypercholesteremia. Thus, in a rabbit with 500 mg. cholesterol per 100 cc. of blood, the effective amount of cholesterol might be 100, 50, or only 10 mg. corresponding to that portion of the cholesterol which is present in large micels. The term "dyscholesteremia" is offered by us as a type of "dyscolloidity." These expressions contrast the normal conditions, eucholesteremia and plasmatic eucolloidity.

Our thoughts regarding the role of colloidal cholesterol are presented in three figures.

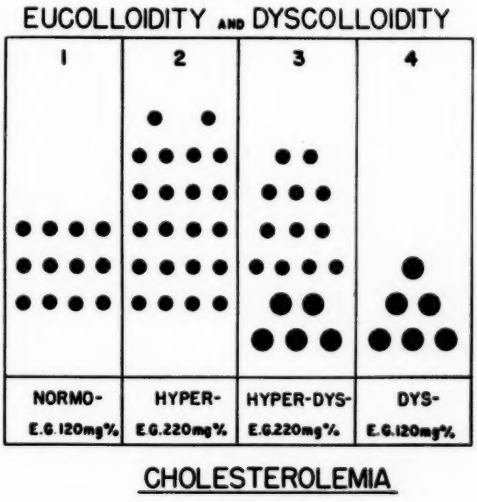

FIGURE 1

Figure 1 depicts four out of six theoretical types of cholesteremia. The small dots represent 10 mg., the large 20 mg. of cholesterol, each. The amount of cholesterol in the first and fourth column is the same; the size of particles differs. The second column picturing micromicels only could be matched by one with only large micels but equal total amount of cholesterol. The third column shows a crude combination of two sizes of particles during hypercholesteremia. A similar condition could be shown during normocholesteremia.

One can hardly expect "pure" forms of cholesteremia with but a single size of micels.

CHOLESTEREMIA

FIGURE 2

In figure 2, four conditions are shown. The first two have an equal, normal cholesterol level, the second two an equal, elevated level. The sample pictures in the second column have more large micels than those in the first. Similarly, there are more large particles in the fourth sample than in the third. The larger number of macromicels in the hypercholesteremic states (3rd and 4th column) reflects the thought that the tendency to formation of giant micels increases with the absolute amount of cholesterol. The lower position of the large dots in the figures indicates their tendency to sedimentation.

We are fully aware of the fact that cholesterol esters rather than free cholesterol are found in atheromatous lesions, both human and experimental. It seems safe to assume that what has been said of free cholesterol is valid for its esterified form, and, for that matter, for all plasma colloids regardless of their chemical structure. One of the common misconceptions concerns the belief that esterification takes place only in the liver. Kawamura (11), Zinserling (22), and especially Versé (20) demonstrated that cholesterol introduced into the subcutaneous tissues is esterified locally. Rohrschneider (18) found this true of cholesterol placed into various parts of the eye. Esterification of cholesterol can take place in the vessel wall proper. In rabbits, this process seems to start about the fifth day after deposition of free cholesterol in the subintimal layer of arteries.

The question arises as to the mode of cholesterol deposition in the vessel wall. It has been stated repeatedly that endothelial cells are not capable of phagocytosis. This seems erroneous. Anitschkow (1), whose name will always be linked with experimental cholesterol-atherosclerosis, injected intravenously various colloids into animals and came to the conclusion that the fate of lipids and of dyes is the same. Both types of colloids appeared simultaneously in the cells known as the reticulo-endothelial system, on the surface of elastic fibers, and in intimal endothelial cells. He called this phenomenon "colloidosis". Our own experiments with injection of colloidal graphite to rabbits substantiate this view.

While it is convenient to speak of a "cholesterol solution" where the micels are so small that they cannot be detected with the optical equipment available, blood cholesterol is always in colloidal suspension. This has been proved by dialysis studies. The dispersion of particles might be so fine that the medium appears clear and that the Tyndall effect is below the measurable threshold.

In our experiments, subintimal foam cells were present mainly in the arterial network nearest to the site of injection. Large micels were precipitated onto the intima promptly. Sedimentation of particles would depend upon their size and weight and also upon the speed of the blood flow. Large and heavy micels roll slowly along the wall while small micels are transported faster, in midstream. These phenomena explain the localization of foam cells in arterial forks, at the orifice of branches, and on the heart valves.

The varying localization of atherosclerotic alterations in different individuals cannot be explained by our experiments, in spite of the fact that we could produce vascular alterations at will in certain organs simply by selecting the proper vessel for injection.

Large micels are precipitated onto the intima and are promptly phagocytized by proliferating

endothelium cells. These cells transform into foam cells. The fact that they are found near the site of the intravascular injection makes it seem unlikely that cholesterol-laden endothelial cells originating in other sites might have found their way into this particular location.

In the course of evolution of medical thinking, atherosclerosis was first considered to be a normal sign of old age, later of aging. Still later it was considered an abnormal process of old age, or of aging. Gradually it became known as a degenerative process not related to any particular age group but more apparent with advancing age. Thus, it was held to be a chronic disease. Our observations suggest that initial atherosclerosis represents an acute defense mechanism to plasmatic dyscolloidity. With repetition of episodes of dyscolloidity the character of atherosclerosis becomes recurrent.

The macromicels responsible for vascular alterations in man most likely contain cholesterol, be it free or esterified. They could consist of pure cholesterol but more likely are of a more complex nature. Lipoproteins, in which the lipid fraction might be represented largely by cholesterol and the protein fraction by alpha- or betaglobulin, seem to be the most likely damaging agents. Some of the macromicels might consist of neutral fat with or even without cholesterol. Or they might not be of lipid nature at all.

Experimentally, lesions indistinguishable from those produced by cholesterol can be initiated by a large variety of macromolecular substances, chemical or bacterial in nature. Theoretically, it seems possible that free or esterified cholesterol is deposited secondarily in defects initiated by nonlipid macromicels. Crystals of cholesterol esters are frequently found in severely damaged or necrotic tissues in which they normally do not occur in appreciable amounts.

Various types of dyscolloidity are illustrated in figure 3. Black dots represent micels of cholesterol and black wedges represent the proportion of cholesterol in a molecule, while empty circles stand for particles without cholesterol. Again, as in the formed figures, only two sizes of molecules were drawn and only four out of numerous possible combinations were depicted.

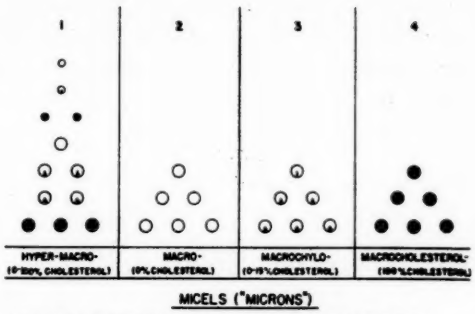

FIGURE 3

In our experiments, initial intimal alterations seemed reversible. Cholesterol reappeared after injection in the blood stream within ten minutes and at the same time it appeared in the liver. An initial phase of hypocholesteremia corresponded, in our experiments, to the period of the primary deposition of the injected material in the blood vessel wall. The gradual rise of the blood cholesterol corresponded to the second phase, the resorption of vascular deposits. As cholesterol was deposited in the liver, the blood cholesterol curve leveled off to the animal's normal value.

The same fluctuations were reported in 1905 by Wuttig (21) for blood fat. Certainly, a portion of the cholesterol will be esterified in the liver. Part of the esterified cholesterol will be eliminated with the bile and part will be reabsorbed into the blood stream. More likely than not, it will reappear in the blood stream in very fine dispersion, in an inert form, and remain so dispersed unless there is hypercholesteremia or hyperglobulinemia and tendency to formation of giant micels.

With multiple insults, especially when these follow in quick succession, the number of vascular lesions increased, in our experimental animals. Holman (9) demonstrated such cummulative character by comparing aortas obtain-

ed at necropsy of individuals grouped according to age. His findings were held evidence of the episodic character of atherosclerosis. One might infer that in older persons the picture represents the cummulative result of intermittent episodes of dyscholesteremia, or, in a broad sense, of plasmatic dyscolloidity.

The next question concerns the possibility that with advancing age dyscolloidity occurs with increased frequency. Becker, Meyer, and Necheles (2, 15) found that chylomicron counts after test meals are higher in older persons than in young ones and also persist longer. Gofman and his associates (6) agree as to hypermacrochylomicronemia after meals but deny that the large fat particles contain cholesterol.

On the other hand, giant molecules with a flotation rate of 10-20 Svedberg units (S_f) containing 30 per cent cholesterol by weight do not increase after a single meal. In a survey of persons of different age groups, one-half of all persons 40 to 70 years old had such giant molecules in their blood, and the incidence of these macromicels was distinctly higher in this age group than in persons 20 to 40 years old. Such giant molecules were found in the blood of rabbits and human beings with atherosclerosis. As a rule, more giant molecules were present in hypercholesteremic blood samples.

Acceptance of the data indicative of an increased tendency or frequency of dyscolloidity with advancing age provokes the question as to the cause of such phenomenon. Becker, Meyer, and Necheles (2, 15) modified postprandial chylomicron curves of older persons by oral administration of pancreatic lipase so that curves resembled those of young persons. Already in 1903 Fischer (5) spoke of the lipolytic activity of blood against neutral fat and cholesterol. He went so far as to say that with disturbance of such enzymatic activity not only is fat not broken down but liposynthesis might occur.

Remesov (17) and Leites (12) pointed out an antagonism between lipase and cholesterol. According to these authors, cholesterol inhibits lipase. Proof of enzymatic aging of man has not yet been given. It has not yet been shown that lipase decreases with age or that antienzymatic action increases with age. The existence of cholesterolesterase, an enzyme esterifying free cholesterol or splitting off free cholesterol from esters, is well known. Evidence of a cholesterolase, an enzyme which would synthetize or degradate free cholesterol itself, is still lacking.

Mayer (13) demonstrated that the colloid-osmotic pressure of human blood plasma rises with advancing age. Colloidal aging of man seems not unlikely. Cholesterol is a hydrophobic colloid and albumin acts as a hydrophilic protective colloid. In order to prepare stable colloidal cholesterol suspensions in blood serum, we had to decrease the amount of globulin and thus increase the relative amount of albumin.

Neuschlosz (16) stated that the more albumin present in a serum the less cholesterol can be extracted from such sample by ether. Gofman and his group (6) ascribed the lower density of molecules with a high flotation rate to a lower protein content of such molecules. Molecules S_f 3-8 contain 25 per cent of protein by weight but S_f 10-20 molecules contain none or very little. Giant molecules were found in the blood of 100 out of 104 patients with myocardial infarction. Specification of the nature of proteins in the giant molecules would be of great importance.

Cohn (4) found in the course of electrophoretic studies that lipoids enter into compounds with alpha- and betaglobulin. He gives the molecular weight of alpha$_1$-lipoproteins as about 200,000 and that of beta$_1$-lipoproteins as over 1,000,000. Alpha and betaglobulins are present in the blood largely paired with lipids. Their relative amount increases with age as the relative amount of albumin decreases.

Discussion of the mode of development of atherosclerosis should be followed by statements relative to the practical implications of our etiologic concept. Preventive, prophylactic, and therapeutic measures will vary with the

etiologic concept to which one subscribes. Those who believe that atherosclerosis is caused by the precipitation of giant molecules of lipoproteins, namely of alpha- and betaglobulin-cholesterol must try to prevent the formation of such giant micels. The attack must be directed against both components of these molecules. If hypercholesteremia is one of the causes of dyscholesteremia, that is, if the quantitative increase of blood cholesterol leads to the formation of large micels, we must try to prevent elevation of blood cholesterol.

While the level of blood cholesterol does not increase after a single meal dietary restriction over a long period of time might influence both the quantitative and qualitative state of blood cholesterol. Gofman and his associates (6) succeeded in reducing the number of giant molecules by dietary measures extended over two to four weeks. Other means of reduction of blood cholesterol must be searched for.

Restriction of fat intake will influence the blood chylomicron count. Investigation of the effect of various diets with varying types of fats might lead to better selection of proper foodstuffs. For the decrease of alpha- and betaglobulin, proper liver function is essential. Dietary restriction of proteins will aggravate the situation. The effectiveness of thyroid preparations and of potassium iodide in the prevention of experimental atherosclerosis and the beneficial effect of these drugs for patients might find its explanation from the fact that iodine combines with globulin and thus prevents its linkage with cholesterol into giant molecules.

While prevention seems most desirable one need not forget possible prophylactic measures. Prophylaxis of atherosclerosis should be based on stabilization of colloids, namely lipoproteins. Bile acids, lecithin, and albumin are three major biologic substances which should be investigated at to their usefulness as stabilizers. Bile acids and salts have not yet been studied sufficiently. In vitro, lecithin appears ill suited as a stabilizer. Mobilization of phospholipids has been recommended by several authors but has not been useful in our hands.

Albumin represents the ideal stabilizer, both in vitro and in animal experiments. Intravascular injection of albumin might theoretically be helpful but practically not applicable. The serum albumin level can be raised by proper diet. The beneficial effect of lipotropic substances, choline, inositol, and methionine, can be explained from the fact that removal of fat from the liver enables this organ to reassume its function as regulator of blood proteins and thus restore the proper balance of protein fractions. (See articles V-VIII of this series. *Geriatrics,* 1951).

Therapeutically, resorption of cholesterol deposits from the vessel wall should be attempted. To date such attempts have failed. Lipotropic agents capable of removal fat from the liver have not been found effective in the removal of subintimal cholesterol deposits. Theoretically, such removal would have to be accomplished promptly after each episode of dyscholesteremia. Even though organization of plaques in man might take more than the thirty minutes it takes in a rabbit it seems likely that it occurs much more rapidly than hitherto thought of. Preventive and prophylactic measures will be more successful than therapeutic attempts.

Summary

1. The macromolecular-colloidal theory of atherosclerosis received support from the authors' experiments.

2. Experimental results lead to the belief that plasmatic dyscolloidity—in a broad sense—can initiate atherosclerotic intimal alterations

3. Experimental results imply that initial atherosclerosis represents an acute defense mechanism of the blood vessels to precipitation of macromicels from the blood stream and that the disease as observed in old age represents the cummulative results of such episodic reactions.

4. Possible preventive, prophylactic, and

therapeutic measures based on the theoretical concepts advanced are presented.

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Differential Decline in the Wechsler-Bellevue Subtests in the Senile Psychoses

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CLINICAL psychologists make use of psychometric patterns of the Wechsler-Bellevue Scale (10) for diagnosis and personality evaluation. Usually this is done without specific reference to the age of the patient. Several investigators, however, have indicated the need to consider the age of an individual in order to compare test patterns. The differential decline in the Wechsler-Bellevue subtest scores with age has been reported on by Fox and Birren (7). These investigators have shown that the normal process of aging accounts for considerable subtest variation.

Balinsky (3) similarly emphasized the age variable in his study which demonstrated increased subtest intercorrelations with age (past 29 years). In simple speed of writing the difference between a control population of "normal" elderly and a matched senile psychotic population has been shown to be statistically significant, but the magnitude of this difference is not as large as that of the difference between high school students and the control population of the normal aged (4). Such results indicate the necessity for having control and experimental samples carefully equated for age.

Rabin (9) reported that there are no significant differences in pattern variations between several senile diagnostic groups, including one of "nonpsychotic." The present study was designed to explore the nature of psychometric scatter in a diagnostic group with the scatter of a control group of normal aged (7). In this way it may be determined which subtests are sensitive to general age changes and which subtests are sensitive to states of intellectual deficit as manifested by senile psychotic subjects. More specifically, the purpose of this study was to compare the Wechsler-Bellevue subtest performance of patients institutionalized for senile psychoses with the performance of a control population of the same age.

SUBJECTS AND PROCEDURE

The subjects of this study were 31 institutionalized patients whose disease was diagnosed as psychosis with cerebral arteriosclerosis or senile psychosis. Each patient was individually examined with the Wechsler-Bellevue Intelligence Scale. All patients were aged 60 to 70 years; all were white and had a minimum of four years of formal schooling. Nativity in each case was the United States or England. Subjects who had a history of functional disorders, organic disorders of exogenous origin, epilepsy, mental deficiency, and vision and hearing too poor to permit valid testing, were excluded. The criteria for subject selection have been described in greater detail in another report (5). This population was matched with the control population (7).

RESULTS

The mean scores of all subtests were lower for the senile psychotic group than for the control group (fig. 1). Tests which showed the greatest decline due to normal aging were not necessarily the tests which showed the largest differences between the groups. Thus the susceptibility of a subtest to age decline does not seem to determine the ability of the subtest to differentiate between control and senile psychotic populations. The information subtest fell within the first two positions when the subtests were ranked in order of their decline. This test which showed little age decline, showed maximum differentiation between the two groups, i.e., by 1.70 σ, using the σ of the control group as the index. On the

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other hand, the vocabulary subtest which also ranked within the first two positions in differential subtest decline, and the digit symbol subtest which ranked last in order, differentiated the two groups by only 0.71 σ and 0.84 σ respectively.

Five subtests differentiated control and psychotic populations by more than one σ; information, picture completion, comprehension, arithmetic, and object assembly (table 1). The subtest which showed the least sensitivity to psychotic deterioration was the digit span subtest. The difference between the 2 groups on this subtest was 0.49 σ. This difference, however, was statistically significant at the 5 per cent confidence level. All other subtest differences in performance between the two groups were significant at the 1 per cent level of confidence.

Discussion

The results of this study show that to evaluate senile psychotic deterioration on the basis of subtest decline, the pattern of decline must be compared to the decline found in control samples of the same age. Without reference to a matched population of the same age, the usual techniques of pattern analysis (8, 10) for the mean results do not indicate a pathologic condition as it exists in the present sample of institutionalized subjects. That is, the information subtest score for the group is higher than the mean verbal score and only about one and a half weighted scores less than the vocabulary score.

Yet it is apparent from the results of this study that when comparison is made with a normal population of the same age, the senile psychotic population suffers a larger loss in information than in any other subtest. In contrast the digit symbol subtest of the control group is below the mean performance score and almost 5 weighted score units below the vocabulary score. Yet, the difference between the two populations for this subtest is only about 0.8 σ.

Vocabulary is ranked first in subtest decline in the senile psychotic population and ranked second in the control population (7). The difference in mean vocabulary scores is only 0.71 σ. Therefore, in relation to the other subtests, vocabulary function may be said to "hold" in senile psychotic deterioration as well as to "hold" in the normal process of aging. The Babcock-Levy Efficiency Index, EI (1, 2) is based on the stability of the vocabulary function. Since the vocabulary decline is relatively small, the score can give an approximation of previous levels of intellectual function.

The data, however, suggest that the Wechsler-Bellevue Deterioration Quotient, DQ, (10) would not be sensitive to both states of normal age decline and to senile psychotic deterioration. Whereas the digit symbol subtest is very age sensitive and the information subtest is not (7), the reverse is true in regard to pathologic deterioration. It is in part for this reason that one study found a correlation between age and DQ (6) and another study found the DQ unable to differentiate between control and senile psychotic subjects (5). It is suggested that the "hold" and "don't hold"

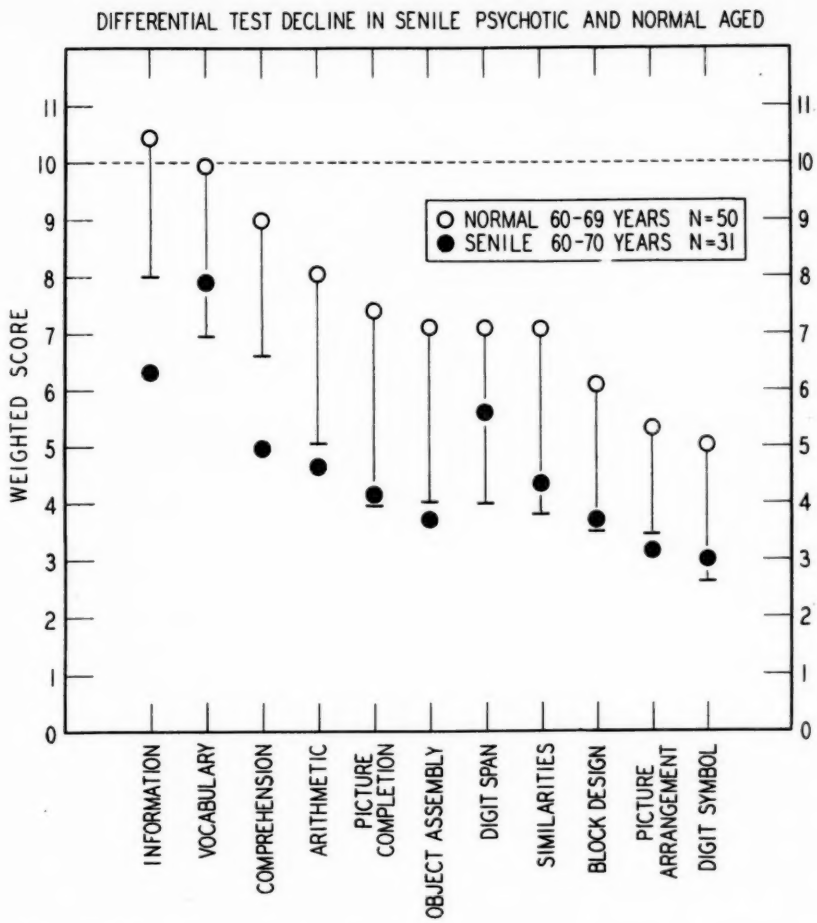

FIG. 1. Mean Wechsler-Bellevue subtest weighted scores. Lower values (●) represent mean scores of a senile psychotic population. Upper values (o) represent mean scores of a matched normal population from data of Fox and Birren (7). Vertical lines (|) represent minus one σ of the control mean. Dashed line (- - -) represents mean level expected in all subtests for a young adult population (from Wechsler, 10).

categories of the DQ are not optimally grouped to measure senile deterioration.

SUMMARY

1. The purpose of this study was to compare the differential Wechsler-Bellevue subtest performance of an institutionalized senile psychotic population with the performance of a control population matched for age, education, race, and nativity.

2. The Wechsler-Bellevue Scale was administered to 31 subjects, institutionalized for psychosis with cerebral arteriosclerosis and senile psychosis. They were free from histories of functional disorders, organic disorders of exogenous origin, epilepsy, and mental de-

TABLE 1. A COMPARISON OF CONTROL AND SENILE PSYCHOTIC POPULATIONS WITH RESPECT TO DIFFERENTIAL WECHSLER-BELLEVUE SUBTEST DECLINE. AGE 60–70 YEARS.

Wechsler-Bellevue Subtests[1]	Rank Order of Decline	Control		Senile		Mean Diff.	Mean Diff. / σ control
		Mean	σ	Mean	σ		
1 Information	2	10.46	2.46	6.29	3.88	4.17	1.70
2 Vocabulary	1	9.96	3.01	7.81	2.78	2.15	0.71
3 Comprehension	4	9.00	2.40	4.97	2.93	4.03	1.68
4 Arithmetic	5	8.06	3.00	4.64	4.30	3.42	1.14
5 Picture Completion	7	7.40	3.35	4.16	3.08	3.24	0.97
6 Object Assembly	8	7.12	3.06	3.71	2.94	3.41	1.11
7 Digit Span	3	7.10	3.12	5.58	2.82	1.52	0.49
8 Similarities	6	7.08	3.32	4.35	2.60	2.73	0.82
9 Block Design	9	6.08	2.56	3.68	2.63	2.40	0.94
10 Picture Arrangement	10	5.32	1.87	3.16	2.64	2.16	1.16
11 Digit Symbol	11	5.02	2.40	3.00	2.38	2.02	0.84

[1]Ranked in order of increasing age decline (7).

ficiency. All subjects had vision and hearing adequate for test purposes.

3. The amount of decline in a subtest with age does not seem to be a criterion of the subtest to differentiate between control and senile deteriorated populations. Only 5 subtests differentiated the populations by one σ or more. These subtests are information, comprehension, arithmetic, object assembly, and picture arrangement.

4. To evaluate senile psychotic deterioration on the basis of subtest decline, the nature of the decline must be compared to the decline in normal aging.

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The Excretion of Pantothenic Acid in Patients with Achromotrichia and Alopecia

VAGN SCHMIDT

ALTHOUGH the importance of pantothenic acid for the maintenance of normal hair in animals seems to have been established, the evidence concerning the significance of this vitamin for the hair growth in human beings is conflicting. While a number of European authors have observed a favorable effect of pantothenic acid in a series of hair diseases, American authors have been unable to find any effects.

Oesch (11) reported favorable results of peroral pantothenic acid administration to patients with seborrheic loss of hair, and Gsell (5) observed improvement in 9 out of 13 patients with slight diffuse hair loss following local pantothenic acid application. Hagerman (7) studied 7 patients with alopecia areata and in 4 of these noted an improvement following pantothenic acid therapy. Favorable results are also reported by Stangl (14, 15), both in patients with hair changes following infectious diseases and in patients with alopecia and achromotrichia. In 10 patients with gray or white hair repigmentation was observed after prolonged local treatment with pantothenic acid.

Juon (8) also noted a beneficial effect of local inunctions combined with administration of pantothenol by mouth. Glanzman and Meier (4) succeeded in obtaining growth of hair in a child with myxedema only after administration of pantothene. Auken (1) noted that local light treatment was unable to produce better results in a number of hair diseases than the administration of pantothene perorally or parenterally.

Other investigators reported lack of effect of panthenol treatment. Vorhaus, Gompertz, and Feder (16), Kerlan and Hervick (9), and Goldman and Mason (6) observed no results from pantothenic acid treatment alone. Brandaleone, Main, and Steele (2) observed no effects on achromotrichia from the combined treatment with pantothenic acid, para-aminobenzoic acid, and brewer's yeast.

Material and Method

If pantothenic acid should have any effect on baldness or gray hair such an effect must supposedly be caused by the alleviation of an existing deficit. In order to investigate this question thoroughly the excretion of pantothenic acid in 115 patients from various hospitals in Copenhagen was studied.

The patients were examined with regard to condition of the hair and were subsequently divided into the following groups: a) patients with normal amount of hair and normal hair color, b) patients with achromotrichia (beginning gray hair, predominant gray hair but with remnants of the normal hair color, and diffuse universal achromotrichia), and c) patients with alopecia. The pantothenic acid content of the diet was estimated by means of a table and in the majority of cases found to be sufficient.

The pantothenic acid content of the urine was determined in a twenty-four hour urine sample, collected before administration of pantothenic acid and again after intramuscular injection of 25 mg. of pantothene. The determinations were made by the technique of Nielson, Hartelius, and Johansen (10).

Results

The results of these investigations are given in table 1. It will be seen from the table that no definite difference can be observed between the excretion in patients with various degrees of grayness or alopecia and the excretion in pa-

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tients with normal hair. The study has thus given no basis for the contention that these patients are suffering from pantothenic acid deficiency which might explain their achromotrichia or alopecia. The urinary excretion figures observed correspond closely to those reported as normal pantothenic acid excretion values (12).

Discussion

According to these observations there seems to be no reason to prescribe pantothenic acid preparations perorally or parenterally in patients with baldness or gray hair. On the other hand, the results presented here do not permit a decision as to whether or not local applications of pantothenic acid preparations are effective.

In a number of experiments on normal rats, Burlet (3) was able to demonstrate that inunction of panthenol produced a local increase in the pantothenic acid content of the skin, both in the treated and in untreated skin regions whereas such application of panthenol was not followed by an increase in the pantothenic acid content of the blood or the urine. Similar inunction experiments in pantothene deficient rats did not, however, produce any increase of the pantothenic acid concentration of the skin. But in these deficient rats an increase of the pantothenic acid content of the liver was noted. From his experiments, Burlet thought it possible to conclude that in pantothenic acid deficiency the body first will saturate the liver with pantothenic acid before an excess is deposited in the skin.

In view of Burlet's observations there should exist a possibility in cases of normal pantothenic acid urinary excretion to increase the pantothenic acid content of the skin by local inunction. If this proved to be the case, the question arises of whether or not such inunction would cause any change in the condition of the hair. This latter problem can only be decided by clinical therapeutic experiments.

Summary

The same urinary excretion of pantothenic acid was found in patients with gray hair and baldness as in normal individuals. There is therefore no evidence that pantothenic acid is an anti-graying factor or is associated with baldness in human beings.

Table 1. Pantothenic Acid Excretion in 115 Patients.

Description	Number of Patients	Age in Years		Spontaneous Excretion in Mg.	Excretion after Loading Dose in Mg.	Increased Excretion in Mg.
		Mean	Range			
Normal Hair	77	31.6	18-48	2.6	6.8	4.2
Achromotrichia[1]	19	46.9	37-60	2.6	7.0	4.4
Achromotrichia[2]	9	55.4	36-70	2.5	7.3	4.8
Achromotrichia[3]	4	60.8	48-72	2.5	7.5	5.0
Alopecia	6	43.5	26-71	2.9	7.9	5.0

[1]Incipient achromotrichia
[2]Predominant gray hair with remnants of normal color.
[3]Diffuse universal achromotrichia.

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The Effect of a Work Program on Adjustment Attitudes in an Aged Population

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Work programs are by no means a novel aspect of institutional operation and maintenance. Certainly such programs, involving as they do the employment of residents, have been tried more or less extensively in homes for the aged. This was particularly so in the much-discredited county poor farm. Can such programs be administered intelligently in such a way so as to benefit the individual as well as the institution in which he resides? Specifically, can a program of work increase materially the personal adjustment of its participants? Evidence to support, at least partially, a positive answer to this question would do much to remove this issue from the realm of speculation.

With this end in view, data gathered in a survey of activities and attitudes of residents of a fraternal home for the aged were analyzed. Results of this analysis show that participants in the regular work program of the institution exhibited better adjustment attitudes than did nonparticipants.

Sample

All subjects in this study were residents of Moosehaven, a home operated by the Loyal Order of Moose for the benefit of its aged and dependent members. Table 1 shows the age breakdown of the sample and of the entire home population at the time of the study. The age distributions for the total home population are given in columns 5, 6, and 7. Since there were only 74 women in the entire group and since usable responses were obtained on less than 80 per cent of this number, it was decided to limit the analysis to the larger male population.

From Table 1 the difference between the *mean* ages of the sample and the population of male residents (columns 4 and 5) is calculated to be .26 years. Since the standard error of the population mean is .358, it is evident that the sample mean lies well within even rigid fiducial limits.

To check on the conformity of the sample age distribution with that of the male population the chi square was computed. Expected frequencies for each of five age categories were estimated from the total male age distribution. All age groups above 85 were combined, thus giving four degrees of freedom. The obtained chi square of 1.51 is well within the limits of chance expectation which gives further indication of the homogeneity of sample and population.

In the sample 61 per cent are workers and 39 per cent nonworkers, whereas 56 per cent of the male population are workers and 44 per cent nonworkers. Again in this respect sample and population are quite similar.

In order to give a fuller picture of the study group other characteristics pertinent to its composition were determined. Thus the majority of male residents in their prime would have been classified as skilled or semi-skilled workers. About one-quarter of the group is Roman Catholic and three-quarters belong to the various Protestant denominations with a few representatives of other faiths.

About 70 per cent of the total population is native-born. Of the remainder approximately two-thirds come from non-English speaking countries. Since most of this latter group immigrated to the United States over 50 years ago, relatively few have any marked language handicap.

The average male in the sample had between six and seven years of schooling. This is approximately one year less than the median of

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7.7 years attained by the United States male population 75 years of age and older.

About one-quarter of the males in the sample are married and living with spouse. Of the remainder, 23.4 per cent were never married, 42.7 per cent were widowed and 9.6 per cent separated or divorced. This distribution of marital status differs markedly from the United States male population over 60 years of age, wherein we find 62.7 per cent married and living with spouse, 10.1 per cent single, 7.1 per cent separated or divorced and only 20.1 per cent widowed.

From this description it may readily be seen that while our sample represents the total population of the home rather accurately in respect to age and work status, in certain other respects it does not reflect the older adult population of the United States.

Work Program

It has been estimated that the part-time work of the residents in this institution would, if taken over by outside help, require the addition of more than 70 full-time employees to the staff of the institution. Thus the economic importance of the work program is obvious. That the work is meaningful as opposed to made-work is indicated by the following list of jobs held by the residents:

Cook	Barber
Kitchen helper	Shopkeeper
Dining room helper	Carpenter
Yard man	Joiner
Janitor	Painter
Watchman	Plumber
Hospital orderly	Meatcutter
Truck driver	Postman
Farm hand	Practical nurse

As would be expected, the majority of the workers hold kitchen, building service, and yard jobs.

Participation in the work program is strongly encouraged but is voluntary. It is obvious to all concerned that the jobs must be done and that each job is an important contribution to the life of the community. While both workers and nonworkers receive allowances, those for the workers are higher and vary with the type of work and amount of time spent.

Method

The adjustment attitudes of both workers and nonworkers were measured by means of an attitude scale devised by Burgess, Cavan, and Havighurst (1, p. 10-11). For this analysis, only parts A through G of the attitude scale were used. Part H, which deals with attitudes toward the family, was omitted in all cases since many of our group had no families and consequently would be unable to answer these items. The attitude inventory consists of seven subsections, each subsection containing seven items to which the subject responds by agreeing, disagreeing or by indicating inability to answer. The subsections deal with attitudes in the following areas: (A) Health, (B) Friends, (C) Work, (D) Security, (E) Religion, (F) Usefulness, (G) Happiness. The scales were scored in accordance with the directions given in the preliminary edition of the examiner's manual.

The instrument was distributed to all members of the home with the exception of a very small number who for physical or mental reasons were patently unable to respond meaning-

fully. Those who for any reason had difficulty in filling out the form were invited to come to the laboratory for assistance. In a few cases staff members helped with the task in the resident's room. No one was forced to respond to the questionnaire but all were encouraged to do so. Responses of varying quality were obtained from 82 per cent of the home population. Approximately one-half of the data was gathered by interview.

Results

Preliminary analysis of results showed that attitude scores of workers were superior to nonworkers for both men and women. Thus the mean score for the male workers was 27.75 as opposed to a mean score of 21.48 for the male nonworkers. The difference of 6.27 between these means yields a t of 6.302. With a t of this size and 169 degrees of freedom we may reject the null hypothesis with confidence (P less than .01). The scores for the women were generally higher than those for men, although again the score for the woman worker exceeded that for the woman nonworker. Thus, 32 women workers received a mean score of 30.00 whereas 14 nonworkers received a mean score of 25.71.

It would be naive, however, to conclude from this that the beneficial influence of work status on adjustment attitude has been demonstrated. Health and age differences between workers and nonworkers must be dealt with before this interpretation can be accepted. Table 2 shows that on a five-point self rating of health nonworkers consider their health to be poorer than do workers. Furthermore, Table 1 shows that the male nonworker tends to be older than the male worker (77.7 vs. 75.7 years).

Thus, in addition to work status, the superior adjustment scores of workers could be attributted to the fact that they thought of themselves as being healthier and that they were in general younger. Since age is never in and of itself a cause of behavior, it need not be considered further in this respect. There remains, however, the strong possibility that the better adjustment scores of the workers simply reflects the better health of that group. It therefore becomes necessary to control or

Table 1. Age Distributions of Sample and Population.

Age	Sample (Male)			Entire Population of Home		
	Worker	Nonworker	Total Male	Male	Female	Total Male Female
1	2	3	4	5	6	7
59 or under					2	2
60–64					5	5
65–69	12	6	*18*	*31*	13	44
70–74	35	15	*50*	*71*	29	100
75–79	34	23	*57*	*82*	20	102
80–84	21	15	*36*	*58*	3	61
85–89	2	7	*9*	*17*	2	19
90–94		1	*1*	*2*		2
95–99				*1*		1
Median	75.7	77.7	*76.5*	*76.8*	72.9	75.8
N	104	67	*171*	*262*	74	336
Mean			76.65	76.91		
σ				5.79		
σm				.358		

Table 2. Comparison Between Workers and Nonworkers on Self-ratings of Health. Ratings of Men and Women Combined.

Rating	Workers		Nonworkers	
	N	%	N	%
Very Poor	4	2.4	13	11.8
Poor	11	6.6	26	23.7
Fair	61	36.3	55	50.0
Good	79	47.0	14	12.7
Excellent	13	7.7	2	1.8
Total	168	100.0	110	100.0

eliminate the factor of health in order to test the hypothesis that no difference exists between workers and nonworkers in adjustment attitudes.

Control of Health. If work status, apart from the effects of health, influences adjustment attitudes, then people of equal health status should vary in attitude in accordance with their work status. There are two general ways in which equated health groups could be formed: use of clinical opinion based upon medical record, and use of the self estimate of health.

Since, in the final analysis health is a difficult thing to evaluate, perhaps the best estimate of this rather indefinite and ill-defined state can be made by the individual himself. Therefore, it was decided to use self evaluations of health as the means of determining equal health status. Consequently our sample of 171 men was divided into three subgroups on the basis of self health estimates. Those who indicated that their health was poor or very poor were placed in Group I; those who indicated fair health in Group II; and those who described themselves as being in good or excellent health in Group III. Reference to table 3 shows that for each health group the mean attitude score is higher for the worker than for the nonworker. Figure 1 represents the data in table 3 graphically.

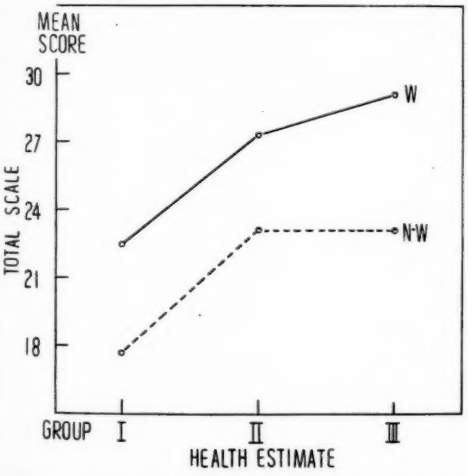

FIG. 1. Relationship between scores on total adjustment attitude scale for workers and nonworkers and self estimates of health: Group I, poor; Group II, fair; Group III, good self-rating of health.

TABLE 3. COMPARISON BETWEEN MEAN ATTITUDE SCORES OF WORKERS AND NONWORKERS BY EQUATED HEALTH GROUPS.

Health Rating		Work Status: Worker	Work Status: Non-worker	Total
Group I Poor	N	11	20	31
	Mean	22.64	17.85	19.55
Group II Fair	N	34	35	69
	Mean	27.26	23.06	25.13
Group III Good	N	59	12	71
	Mean	28.98	22.92	27.96
Total N		104	67	Grand Total 171
Health Rating Mean		27.75	21.48	Grand Mean 25.29

Table 4 shows an analysis of variance of these data in which the distortion created by the unequal and disproportionate subgroup

TABLE 4. ANALYSIS OF VARIANCE CORRECTED FOR DISPROPORTIONALITY (2).

Source	Degrees of Freedom	Sum of Squares	Variance
1. Between groups			
Work status	1	1613.53	1613.53
Health	2	737.29	368.64
Interaction	2	21.89	10.94
2. Within groups	165	5415.04	32.81
Total	170	7787.75	

$F_{\text{Work Status}} = 1613.53/32.81 = 49.18$ (P less than .001).

$F_{\text{Health Rating}} = 368.64/32.81 = 11.24$ (P less than .001).

numbers has been corrected (2). This analysis clarifies three points:

1. The F ratio for work status indicates that the difference in adjustment attitude scores between workers and nonworkers is not a chance occurrence and is not an artifact created by the health difference between the two groups. Thus the fact that a resident is working is in and of itself an aid to his adjustment as measured by the instrument used in this study.

Since it may be argued that these results can in part be accounted for on the basis of selection, a further study of the nonworkers was made. This analysis showed that the 18 nonworkers who had never held a job in the home earned a mean adjustment attitude score of 21.11, while the 49 nonworkers who had "retired" from the work program earned a score of 21.61. If there existed a marked tendency for only the better adjusted oldsters to seek work, then we might reasonably expect a difference in adjustment attitude to obtain between these two groups of nonworkers. Since the difference between the two groups is negligible and can be accounted for on the basis of chance, it seems entirely reasonable to conclude that it is participation in the work program which produces the differences obtained between the worker and nonworker groups, rather than some factor related to selection.

2. The F ratio for health indicates that the differences in attitude scores between the various levels of health cannot be accounted for on the basis of chance. Thus the individual's estimate of his own health influences the adjustment attitudes measured by the scale under discussion.

3. A third point of importance is that no interaction exists between work status and self health rating. This is indicated by the very small interaction variance in table 4. Therefore, when workers are compared to nonworkers, the degree of difference between the resulting mean adjustment attitude scores is independent of the health classification. It is suspected, however, that when subscores of the attitude tests are considered in some at least an interaction may be present.

Figures 2 through 8 show the relationship between health status and subtest scores on the adjustment attitude inventory. These graphs show the average attitude score for workers and nonworkers in each of the three

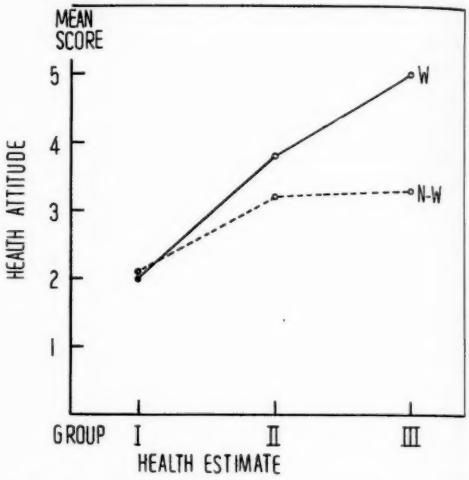

FIG. 2. Subscale A. Attitude toward personal health.

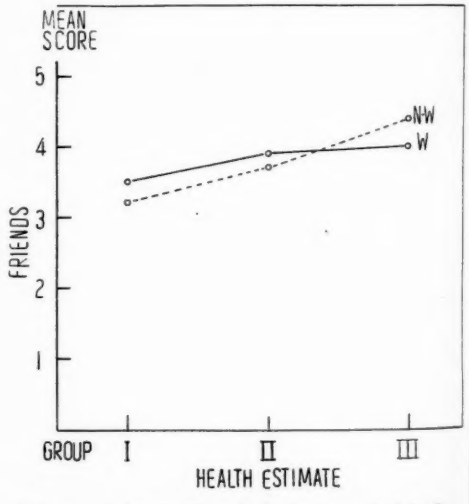

FIG. 3. Subscale B. Attitude toward friends.

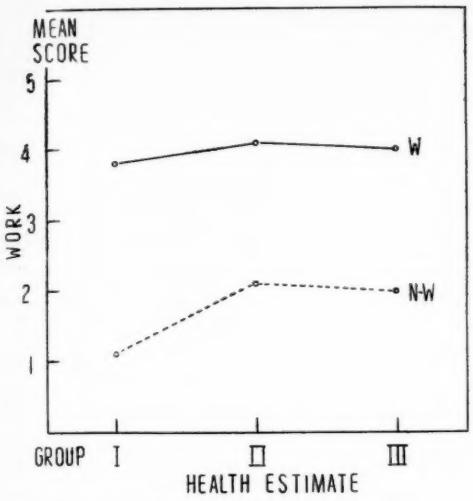

FIG. 4. Subscale C. Attitude toward work.

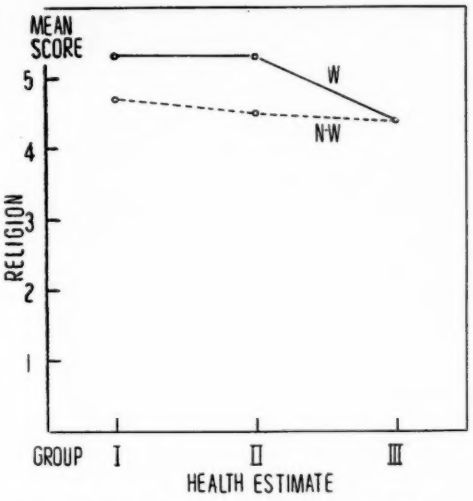

FIG. 6. Subscale E. Attitude toward religion.

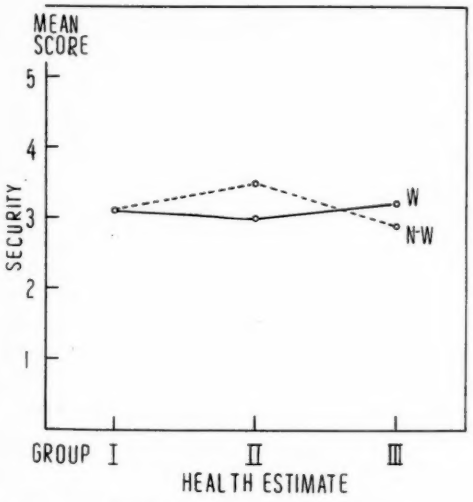

FIG. 5. Subscale D. Feelings of security.

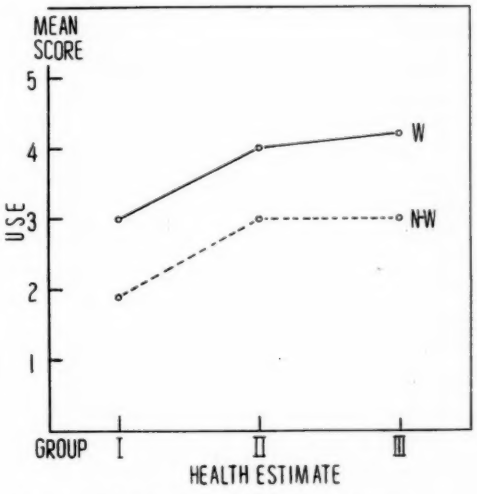

FIG. 7. Subscale F. Feeling of usefulness.

health groups: (I) Poor, (II) Fair, (III) Good. Thus in figure 2, we see that the health adjustment attitude scores for those who rate their health as being *poor* are practically the same for both workers and nonworkers. However, for those who rate their health as *fair* or *good* the workers have a higher average score than do nonworkers.

While no interaction can be demonstrated between health and work status when total attitude scores are considered, examination of figures 2 and 8 (Health and Happiness) suggests the possibility of interaction in these two subscales. If this hypothesis could be substantiated, it would suggest that as health rating increases the differences between the work-

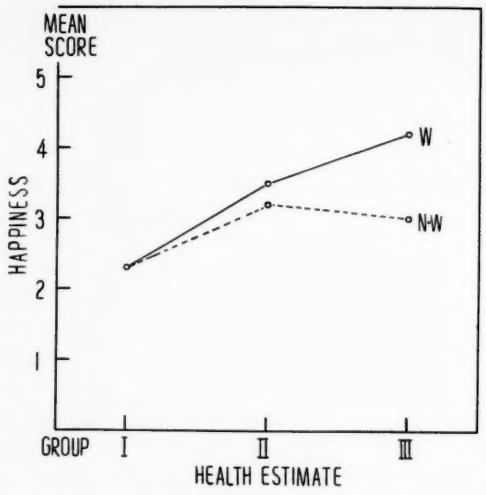

FIG. 8. Subscale G. Feeling of happiness.

ers and nonworkers on these two variables also increase.

The largest differences between the workers and nonworkers are shown in figures 2, 4, 7, and 8, representing subscales for attitudes in the area of health, work, feelings of usefulness and happiness. Chi square was calculated for the distribution of scores for each of the subscales in order to test the hypothesis that both the worker and nonworker scores were drawn from the same population of scores. This hypothesis was found untenable for subtests (A) Health, (C) Work, (F) Usefulness, and (G) Happiness. In each of these cases P was less than .001. The hypothesis was substantiated for subtests (B) Friends, (D) Security, and (E) Religion. On each of these subscales the distribution of scores for workers and nonworkers differed only in accordance to chance expectation (P = .20 or higher).

Thus the difference in adjustment attitude scores between the workers and nonworkers shown in figure 1 and in table 3 can be accounted for primarily by the differences in attitudes between the two groups expressed on subscales concerned with attitudes towards health, work, usefulness, and happiness. Workers in the study group feel healthier, have better work attitudes, and have greater feelings of usefulness and happiness than do the nonworkers.

DISCUSSION

It is of course recognized that only limited generalizations can be made on the basis of these data because the study group represents a random sampling primarily of the population of but one institution. Be that as it may, these results are a substantial indication that the work program at this particular home contributes something over and above the mere doing of necessary jobs. We are led to accept, with more than casual confidence, the evidence that the work program does aid directly the happiness and adjustment of those who participate in it. For those who see the program in daily operation there is no difficulty in appreciating its contribution to the personal adjustment of the workers. It is much more difficult to convey this impression to those who cannot observe it but who nonetheless want facts.

These findings are of value in that they present a comprehensive picture of the attitudes of a large and representative group of participants in the work program. They show that the adjustment attitudes in this group are superior to those who do not participate in the program and thereby emphasize the adjustment values of meaningful, voluntary work.

SUMMARY

An adjustment attitude inventory was given to a group of resident workers and nonworkers in a fraternal home for the aged with the following results:

1. Workers obtained higher adjustment attitude scores than nonworkers of comparable health status.

2. Both workers and nonworkers who rated their health good or fair obtained higher ad-

justment attitude scores than those who rated their health as being poor.

3. Workers earned higher scores than nonworkers on subscales of the adjustment attitude inventory dealing with the areas of health, work, feelings of usefulness and happiness.

Acknowledgement is made to Mr. Robert W. Arms and Dr. George E. Myers for their work in the collecting of data and to Dr. Walter D. Obrist for his critical discussion of procedure and of results.

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Social Roles in the Prevention of Senility

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SENILITY has social and psychologic manifestations based only in part on the aging of the body. People are described by their personality characteristics and are frequently called senile when they are advanced in age and have become eccentric, careless, or absent-minded. They are also judged by what they do, the roles they take in every-day living. These observations have led to further investigation to find out how active old people are in various social roles and how these activities relate to youthful or nonsenile personality patterns of people over 65 years of age. This information is necessary in order to understand social aspects of senility and to find an approach to possible methods of preventing the development of undesirable social patterns and personality characteristics.

METHODS

Two measuring instruments were devised for this study and a third one was adapted:

1. A Role-Activity Scale was constructed to rate activity on a 10 point scale within the 12 role-areas given in table 3. Additional scales measured prestige, financial condition, and the status of the individual.

2. The Cavan Scale of Adjustment Ratings for Later Maturity (2) was used to rate the degree of integration into social life and the attitudes significant for adjustment in these years. A single master rating was used as the adjustment score for each subject.

3. The Personality Register was devised to rate elderly people on characteristics generally ascribed to aging (table 1). Five stages of manifestations each with 2 rating points were outlined for each of the 6 characteristics. This gave the rater an opportunity to place each subject according to the relative strength or weakness of that characteristic.

By the proportional stratified sampling method 100 subjects were selected, representing a Midwestern community population of people over 65 according to age, marital status, and social class position. Information was obtained by interviewing each subject. The schedule, Your Activities and Attitudes (1), was used for detailed information, and the focused interview (3) for deeper feelings and attitudes. Additional information of value was gathered from newspapers, observations, membership lists, and other local sources.

Subjects were rated by at least three judges on each role-activity, the adjustment scale, and on the Personality Register. Scores were evaluated separately and were also combined into one composite activity, personality, and adjustment rating for each individual.

RESULTS

Condensed descriptions of low, medium, and high personality patterns of old people showed the following distribution in the sample:

1. At the bottom of the scale were the people described as cantankerous, irascible, self-centered, and unable to get along with others. They wanted their own way and met problems by childish or impulsive means. They lived from day to day, were absent-minded, or had their interests centered in the past. They vegetated; did nothing even though their physical condition did not prohibit activity. They were unhappy; did not enjoy people or any social and recreational activities. They also gave little or no attention to their appearance.

Eleven per cent of the sample were rated in this group. Some of them were considered senile in home-town language because they were becoming more and more withdrawn and several were in need of institutional care.

2. The second group was family-centered,

TABLE 1. REGISTER OF PERSONALITY CHARACTERISTICS OF THE AGED.

0–1	2–3	4–5	6–7	8–9
Altruism				
Cantankerous, with little or no expression of good will.	Grudgingly gives help to others when asked.	Family centered; little expression of good will outside of family.	Kind and good but needs stimulation, e.g. church, disaster, etc.	Benevolent, kind, and good to others without being stimulated by outsiders.
Approach to Problems				
Impulsive; does not stop to think about outcome.	Meets problems as per habits of former years. Immature.	Usually objective approach to problems; sometimes impulsive.	Weighs problems; keeps away from personal feelings most of the time.	Judicial attitude; always objective.
Time Centered Interests				
Lives from day to day; never plans ahead. Mind centered in the past.	Seldom plans ahead. No plans for coming year, or next day.	Plans ahead, but only for short time; home and business centered.	Plans and interests deal with self, home and community within a year.	Thinks in the future; has varied plans and interests of long time range.
Mental Stimulations				
Vegetates; does nothing even though he could.	Spends little time on hobbies and other activities.	A few hobbies and/or other varied activities.	Moderately active and interested in new or present projects.	Very active, interested and busy. Always has new projects to start.
Friendliness				
Unhappy; does not enjoy people or social and recreational activities.	Dislikes meeting new people. Does not like social gatherings of more than three people.	Visits occasionally. Secure only in own group.	Makes new friends easily; enjoys social life.	Meets people well; enjoys social life, goes to parties, entertains, and visits.
Interest in Appearance				
Sloppy, with little or no attention to appearance.	Some attention to appearance; not always clean.	Neat and clean but little or no attempt at adornment.	Always neat; not always in style, but tries to look nice.	Great pride in appearance; hair well kept; clothes well cared for and in good taste.

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with little or no expression of good will outside of the family. These people were usually objective in their approach to problems, but impulsive at times. They planned ahead for only a short time and tended to center plans around their home and business activities. They had few hobbies or variations in activity. They visited others occasionally but felt secure only in their own group. They were neat and clean but made little or no attempt at adornment.

Fifty-four percent of the sample were in group 2.

3. The people at the top were altruistic, kind and good to others without special stimulation. Their attitudes were judicious and they were mainly objective about their problems. They had varied plans and interests and tended to project their thoughts to the future. They were very active, interested, and busy; always had new projects to start but were not just "running away." They met people well, enjoyed social life, went to parties, entertained, and visited others. They took great pride in their appearance; hair and clothes were well cared for and in good taste.

Thirty-five per cent belonged in this group. Comparable ratings were not available for younger people but the description just given could fit many people in their twenties. This group was three times as large as the senile one. Some of the people were so trim, youthful, and alert that special questioning was necessary to establish the fact that they were actually over 65. Similarly, some people in their eighties who ranked high on the personality scale seemed more agile mentally and more social-minded than many people in middle-age.

The relationship between characteristics was evaluated by product moment correlation coefficients. All of the correlations, as given in table 2, were significant at the 1 per cent level. The highest relationship was between mental stimulation and time-centered interests ($r = .86$). Individuals who had many activities and a stimulated mind tended to have interests in both the present and the future. Conversely, persons with few interests frequently lived in the past and repeated stories of their youth over and over, or were very forgetful. The lowest correlation ($r = .43$) was between interest in appearance and friendliness. Some of the men were very friendly but, unless supervised by a woman, tended to be negligent about their appearance.

TABLE 2. CORRELATION COEFFICIENTS BETWEEN PERSONALITY CHARACTERISTICS

Personality Characteristics	Altruism	Approach to Problems	Time-Centered Interests	Mental Stimulation	Friendliness	Interest in Appearance
Altruism						
Approach to Problems	.56					
Time-Centered Interests	.57	.45				
Mental Stimulation	.60	.63	.86			
Friendliness	.71	.64	.57	.63		
Interest in Appearance	.48	.47	.68	.65	.43	

Comparison of individual characteristics showed that after the age of 65 women tended to be more altruistic and kind than men, but men tended to be more judicious. Men and women were similar in time-centered interests and friendliness. Women rated somewhat higher than men in amount of mental stimulation and very much higher in their interest in appearance. On the whole all of the factors were rather closely related as far as individuals were concerned, so the composite score was used for further analysis.

TABLE 3. PERSONALITY PATTERNS AND SOCIAL ROLES.

Social Role	Correlation with Personality	Characteristics of a Low Personality Score	Characteristics of a High Personality Score
Parental	0.51[1]	No children. Lost track of children. Were dependent upon children.	No children. Independent of children.
Grandparents Great-grandparents	0.47[1] 0.69[1]	Some: Close social and affectional relationships. Others: Little information about descendants.	Close social and affectional relationship with all descendants.
Home Conditions	0.44	Lived alone or in Old-Age Home.	Lived with spouse; no children in the home. Lived alone.
Kinship	0.48	Had no relatives. Were not in close touch with relatives.	Visited relatives frequently; fairly close affectional ties.
Social Clubs	0.58	Never belonged to any social organization.	Tendency toward high social activity. Some were members in two or more clubs.
Business Clubs	0.39[1]	Never belonged to any union or business clubs.	Only nominal members; limited interest in business organizations.
Church	0.38	Dropped out of church group years ago. Reduced church attendance.	Active church members. Very devout; home services or listened to radio religious programs.
Peer Participation	0.52	Few individual friendships. Visited friends infrequently.	Many acquaintances and several very close friends. Visited friends frequently.
Clique Activities	0.57	Belonged to no clique or small intimate groups.	Associated in cliques or in small intimate groups.
Civic Activities	0.50	About half of them voted in the elections. Others took no interest in any civic affairs.	Took an active interest in civic and community affairs.
Job Activity	0.44[1]	Some worked spasmodically. Others had given up work willingly.	Men were working. Women were employed or were homemakers.

[1]N = 100 except: Parental N = 78, Grandparent = 70, Great-grandparent N = 23, Business Clubs N = 48, Job = 53.

The personality score and the adjustment scores showed a product-moment correlation coefficient of 0.85, indicating that the individual with a youthful or nonsenile personality pattern also tended to be well adjusted. Personality scores and the total role-activity score correlated 0.77. People who were active and had responsibility also tended to have an adult

or nonsenile personality in contrast to the senile type. Inactive aged tended to show the characteristics generally ascribed to aging.

Individual social roles were evaluated in terms of the personality ratings and showed the distribution and relationships given in table 3. The people with a high personality rating showed certain communalities in their way of life. They were independent of their children and had allowed their children to become independent; none had children living in their home. They had established close social and affectional ties with all descendants. Kinship ties were close but they did not depend only upon relatives for social life. All of them were active in organized social clubs but were also members of nonorganized, informal cliques. They had individual friends of various ages and took the initiative in making new friends. Some were fairly active in civic and community affairs but all voted in the elections. All of the men and some of the women were still working and enjoying it.

High financial security was not necessarily related to desirable personality patterns in advanced years; some of the wealthy were cantankerous or had many of the characteristics of old age; some of the poor were still youthful in spirit. The most favored group was the one with enough economic security to meet needs comfortably.

Prestige and status in the community were favorably related to the personality patterns of the individual. These were built up during the years and were possibly influenced by the personality of the individual in the first place.

Personality in Social Classifications

Distributions according to marital status, social class, and age-grading were studied to find the effects of these factors on personality in old age. Comparison of mean scores showed the following statistically significant differences between mean ratings:

Age-graded scores in five-year stages showed no significant differences for either men or women in any age comparison; not even between people 65 to 69 and people over 80 (table 4).

Age means tended to be similar because some people in each five-year age group had high ratings; others rated low regardless of age. Health could not be credited or blamed for this directly; low rating subjects reported health conditions ranging from perfect to seriously ill. A fairly high death rate reduced the piling up of senile cases in later years. Actually, people over 65 who had high personality ratings had always been active, continued to be so, and avoided getting rusty by having a variety of activities and interests.

Marital status distribution of personality ratings are shown in table 5. Comparison of means within the same sex group showed that married men had significantly higher scores than either widowed or single men. Married women rated significantly higher than widowed women only.

Social and cultural factors must be recognized for their specific influence on personality traits. Our culture favors married people; they have a two-way entrance into the social

Table 4. Personality Score Means by Sex and Age.

	Age 65–69		Age 70–74		Age 75–79		Age 80+	
	No.	Score	No.	Score	No.	Score	No.	Score
Men	17	4.77	13	4.85	7	4.29	8	4.75
Women	19	5.47	15	5.20	13	4.85	8	4.88

TABLE 5. PERSONALITY SCORE MEANS BY SEX AND MARITAL STATUS.

	Married		Widowed		Single	
	No.	Score	No.	Score	No.	Score
Men	28	5.32	10	3.8	7	3.57
Women	17	5.88	33	4.82	5	5.0

life of a small community. Women usually plan the social functions for the family. This was probably one reason widows withdrew somewhat from social life, but widowers were "lost" and showed personality patterns of lower rank than they had while married. In spite of the small number of single people some factors seemed important: Few women in the lower classes remained unmarried so the single women in this study were of higher social class than the single men. Most of the single women were working and were active in the social life of the community; single men tended to withdraw even from church activities.

Social class position was obtained by Warner's Index of Status Characteristics (4). Upper and upper middle class people were grouped together because the numbers in both were small. The distribution, showing personality means, is listed in table 6.

Upper and upper middle class men had scores similar to those of lower middle class men, but rated significantly higher than both upper and lower lower class men. Business men, skilled workers, and comfortably retired farmers had higher ratings than did men of lower occupational rank. They had no more education than the lower status group but utilized their intelligence in a different way; they read, worked, traveled, and had social interests to keep them alert.

Among the women the ratings of lower lower class groups were much lower than ratings for all other classes. No other interclass comparisons were significant.

DISCUSSION

People with nonsenile personality ratings had learned social, job, and recreational skills earlier in life. Prevention of special characteristics seemed also to be centered in the earlier years. Altruism, the interest in others, and habits of friendliness were started in childhood: methods of meeting problems and emotional maturity depended largely upon practice and success in facing problems throughout the years; projection of interests was possible with enough energy, intelligence, and stimulated curiosity; and even pride in physical appearance was aided by learned self-responsibility and interest in being accepted by others.

This was only an exploratory study, and further research is needed to learn more about the factors that cause some people to become senile and allow others to remain active, mentally alert, and pleasant despite the years.

SUMMARY

The social roles, personality characteristics, and adjustment patterns of people over 65 were rated on specially designed scales. The 11 per cent who rated low on the Personality Reg-

TABLE 6. PERSONALITY SCORE MEANS BY SEX AND SOCIAL CLASS.

	Upper and Upper Middle		Lower Middle		Upper Lower		Lower Lower	
	No.	Score	No.	Score	No.	Score	No.	Score
Men	7	5.71	12	4.83	17	4.65	9	3.89
Women	11	5.28	19	5.79	20	5.1	5	3.6

ister were relatively inactive and rated low in adjustment. This group included subjects popularly considered senile. Fifty-four per cent rated in the center of the scale, and thirty-five per cent rated high, were alert, and had youthful personality patterns.

Social factors found in nonsenile patterns seemed to center around: 1. Active social roles, especially having a family but not depending only on family members and relatives for social life, 2. Association with other people in groups and individual relationships, 3. Interest in a variety of activities, 4. Interest in the future, 5. Marriage, 6. Middle class status, and 7. Continued work.

Personality factors included: 1. Good adjustment in childhood and throughout life, 2. Ability to meet problems, 3. Good relationships with other people, and 4. Development of wholesome attitudes during childhood.

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CURRENT COMMENT

Aging

Oscar R. Ewing, Federal Security Administrator, has announced the initiation of a new publication in the field of gerontology and geriatrics, *Aging*. "*Aging* is a medium for sharing information about programs and activities among agencies and organizations in the field, their staffs and board members, and other interested individuals. It will be issued without regular schedule as significant material is available and distributed without charge." The first issue is dated June 18, 1951.

Communications and items thought to be suitable for publication should be sent to Clark Tibbitts, Chairman, Committee on Aging and Geriatrics, Federal Security Agency, Washington 25, D. C.

Argentine Gerontological Society

The Sociedad Argentina de Gerontología y Geriatría has been formed in Argentina. It is devoted to the promotion of the study of the physiology and pathology of the aged and aging as well as to the prevention and treatment of the diseases of old age.

Dr. Ernesto A. Rottjer is President; Dr. Benjamin Spota, Vice-President; Dr. Miguel C. Lacalea, General Secretary; Dr. Domingo Passanante, Assistant Secretary; and Dr. Osvaldo Fustinoni, Treasurer. Correspondence should be addressed to Dr. Miguel C. Lascalea, Sarmiento, 2691-3A, Buenos Aires.

Gerontological Unit

A new Gerontological Unit has been established at the Mental Health Institute, (Dr. W. C. Brinegar, Superintendent) 1200 West Cedar Street, Cherokee, Iowa, under the directorship of Dr. Raphael Ginzberg.

The goal of the Gerontological Unit is: to study the condition and needs of the mentally ill as well as those elderly people who are presumably healthy; to conduct these studies from the medical and psychiatric as well as psychologic and socio-economic aspects; to introduce modern geriatric methods of treatment into mental hospitals; to rehabilitate those mentally sick elderly who can be cured or improved and decrease thereby the elderly population of mental institutions.

At the present time surveys are being conducted by the Unit in preparation for geriatric in- and out-patient hospital work.

Program of Courses for Older People

The Department of Adult Education of the Los Angeles City Schools announces a year's program devoted to problems of older adults. This program will be carried out in cooperation with the Los Angeles County Committee on Needs and Opportunities of the Aged and other agencies interested in senior citizens during the period, October 9, 1951, to June 1, 1952. The course will be held as evening classes and are primarily designed for people over

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The hieroglyphics, "The Beginning of the Book for Transforming an Old Man into a Youth," at the top of this editorial page, are from the Edwin Smith Surgical Papyrus, translated by Professor John Breasted, University of Chicago Press.

60 years of age. The topics to be covered include foundations for enriched living, health, management of personal affairs, diet and nutrition, psychologic aspects of aging, and crafts hobbies and creative activities.

News and Notes

An all-day "Conference on the Care of the Aged and Chronically Ill" was held under the auspices of the Baltimore City Medical Society in Baltimore on Wednesday, June 27, 1951. The Conference under the chairmanship of Dr. Herman Seidel was planned to give physicians, nurses, social workers, and administrators associated with nursing homes and homes for the aged an opportunity to discuss their mutual problems.

The North Carolina Conference on Aging, a citizens' conference called by Governor W. Kerr Scott, was held at the Sir Walter Hotel, Raleigh, North Carolina, June 28-29, 1951. Problems of the aged in the fields of religion, education, recreation, employment, health, research, personnel, and social service were discussed.

Governor Warren of California has called a Conference on the Problems of the Aging for October 15 and 16 in Sacramento. This is to be a statewide conference to provide a large group of representative citizens the opportunity to explore and identify the problems raised by the presence of an increasing number of older persons in the State's population. It is expected that this group will make recommendations for ways and means of solving these problems. The Conference is to be set up with the following major divisions: Employment Opportunities, Income Maintenance, Physical Health, Mental Health, Education, Social Welfare Services, Recreation, Housing and Living Arrangements, Community Organization.

In addition, there will be a Research Division, the members of which will sit in on the meetings of all the sections of the previously mentioned divisions. They will then make recommendations for needed research projects, legislation, and fiscal requirements.

Emphasis is being placed on the fact that this is to be a citizens' conference and not a conference of state officials. Similarly, emphasis will be placed on the major responsibility of each community to face its own problems raised by its elder citizens and to utilize its resources to meet the problems. State departments and their staffs will be available for consultative services and other required types of assistance.

Inquiries should be directed to Mr. Louis Kuplan, Conference Executive Secretary, 616 K Street, Sacramento, California.

Two courses, Problems and Adjustment of the Aging and Aged in Contemporary Life, and New Developments and Resources for the Aging and Aged in Contemporary Life, given by Mrs. Ruth Laverty in 1950 and again this year July 2-20 and July 23 to August 10 are being repeated September 24, 1951 through January 31, 1952. Inquiries should be addressed to Associate Professor Esther M. Hilton, School of Education, New York University, Washington Square, New York 3, New York.

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Gerontologic Topics in Finnish Medicine

Few investigations deal solely with gerontologic problems, yet most studies contain some observation of gerontologic interest. Thus when Rouhunkoski (7) studied the relation between thyroid function and the existence of uterine myomata, he found that the age factor must be taken into consideration. The incidence of thyrotoxic symptoms in his series seemed to increase with age. He examined the iodine tolerance test in this connection, failing, however, to demonstrate any relation between the 6-hour values and the age of the patients.

Vehaskari (20) has studied sterility in Finnish women, its causes and prognosis. He examined the incidence of intramural and isthmic tubal occlusions in relation to the age of the patients. On basis of 821 salpingographies he arrived at the conclusion that the increase in the incidence rate in older age groups was so slight that it is not justifiable to ascribe sterility in elderly women mainly to the existence of these occlusions. When a comparison was made in relation to the prognosis of sterility in different age groups, a steady aggravation with increasing age was noted, yet, even in the age groups 36 to 40 years the percentage of patients who became pregnant was 28, a figure obtained after exclusion of untreated cases and cases rendered incapable of reproduction by operation (amput. uteri, sterilization, etc.). In view of this finding, the author states that it is not possible to establish a limit outside of which—within the period of fertility—the prognosis of female sterility has to be considered beyond hope.

The prognosis of sterility was apparently related to the age of menarche, being possibly somewhat poorer in the group of women with high age of menarche. The rates for pregnancies were namely 26.5 ± 2.8 per cent when the age of menarche was less than 14 years, and 20.5 ± 3.1 per cent when it was over 16 years, (unreduced values, i. e., cases rendered incapable of reproduction included).

Vara has studied the social and obstetric problems connected with old primiparae age $\geqq$ 30 years, (17). The material comprised 19,216 first deliveries with 3537 mothers over 30 years of age. In 1927 approximately every tenth primipara was an old one, in 1941 every fourth.

The operative incidence 23.9 per cent of full-term deliveries in old primiparae was nearly 50 per cent higher than in young primiparae; this also holds true for the incidence of weakness of pains. The average weight of the child was definitely greater in old than young primiparae. No difference in the maternal mortality was, however, discernible.

An immense shift in the sex ratio was noted in the children of mothers over 40. Instead of being 107 as for the whole material, this ratio showed an increased preponderance of males, amounting to 137.

Infant mortality and the incidence rate of soft-part ruptures, severe nephrogestations, eclampsismus, and eclampsia, was higher in the old than in the young primiparae. Because of these complications the author concludes that an "old" primipara should always have institutional care.

In a study on late second childbirths (18), with an interval between first and second deliveries of more than five years, the same author could find no difference in the prognosis for child or mother due to the long interval between successive deliveries. The incidence of operative deliveries is not higher in late II-parae than in II-parae in general, except for the cases in which the interval was more than fifteen years. Yet, the percentage of women over 40 years old in the late II-parae was 3.5 times as high as among II-parae in general.

The fear among parturients that childbirth might offer special difficulties if a long interval had elapsed between deliveries therefore seems unfounded, except for those cases in which the interval exceeded fifteen years.

Pitkänen (6), in an investigation dealing with the relation of incisional herniation to previous operations for appendicitis with peritonitis, has found that the predisposition to incisional herniation increases with advancing age in women but not in men. Since intellectual workers also have a greater disposition to hernia than laborers, the author concludes that accumulation of fat and weakness of the muscular abdominal wall may be responsible for the greater disposition to herniae in general, and particularly in old postmenopausal women.

Several authors have treated certain hematologic problems from a gerontologic point of view. Sievers (14) endeavors to determine whether agglutinating substances of red blood corpuscles are present from the outset, or whether these substances are formed during the ripening time of the erythrocytes. The erythrocytes of the youngest type, (Group I, Heilmeyer) are not affected by isoagglutinating sera. Thus isoagglutinability only develops during the ripening process.

Åberg and Tötterman (21) have studied the white blood picture in 122 individuals over 60 years old. No conspicuous difference between young and old people could be detected by routine differential counting methods. The only difference was found in the incidence of an increased number of nuclear segments in the neutrophiles, there being in younger adults an average of 2.73 segments, in patients with pernicious anemia 3.84, and curiously enough, nearly as many, vix., 3.77, in those of old people.

Hernberg (3) found in an investigation on the variations in the blood hemoglobin level, erythrocyte count, volume, diameter, and thickness of erythrocytes in different age groups, that the diameter shows a small but significant regular increase with age, except for babies 1 to 14 days old, a group in which the average diameter (up to 8 μ) is largest. Setälä (13) determined the hemoglobin content of blood in 70 per cent of the total population of a rural district in Southern Finland during the one year period 1945 to 1946. The age groups from 0 to 89 years were represented. As a mean value, 13.43 ± 0.04 for adult males and 12.05 ± 0.03 for females respectively was found. The values decreased slightly with age, being 12.3 and 11.4 in the oldest age groups.

Sarvilahti has studied the incidence of both exudative pericarditis (10) and that of adherent pericardium and constrictio cordis (11) in an autopsy material comprising 3054 cases. In 59 cases (1.9 per cent) an adherent or thickened pericardium was found. Etiologically the dominant group was that of cardiosclerosis. This implies that the disease is found more often in patients past 50 than in young people. Thus it forms a striking contrast to exudative pericarditis, which is a disease predominating in children and young adults. On the other hand, all severe cases in which constrictio cordis was presumably the cause of death were found in men 15 to 35 years old.

The adhesive pericardium in this series was never diagnosed intra vitam.

Halonen and Halonen (2) have made a statistical study concerning the incidence of urinary tract infections in women. The incidence rate was slightly increased in the decade 50 to 59 and more so in old women over 70. Sauramo (9) made a survey of postmenopausal affections in women and their statistical distribution in a clinical series collected from the Womens Clinics of the University.

Brummer (1) investigated the age of death of parents to hypertensive patients and compared the mean age of death with the mean age at death of parents to normotensive patients. The material displayed a somewhat lower mean death age of mothers but not of fathers to hypertensive patients.

A paper by Vartiainen and Kanerva (19) deals with the problem of arteriosclerosis and nutrition. The authors have compared the incidence of arteriosclerotic vascular changes of different degrees in two strictly similar autopsy materials compiled from pre-war and war-time periods. The age groups under 20 years were excluded. The result was indicative of a strikingly favorable effect of the restricted diet of war years on arteriosclerosis.

The total incidence of arteriosclerosis was definitely less during the war-years 1939 to 1944 than in 1933 to 1938. The difference was most pronounced in the group of 30 to 39 years old. The group 20 to 29 and those over 80 years old did not show any difference and in the group of 70 to 79 years the reduction was only slight. When a comparison was made between the incidence of lesions of the same degree, the result was as follows: The 30 to 39 year group showed a slight decrease of mild lesions (yellow intimal spots) but in the older subjects no significant change was noted. For more severe lesions, however, the reduction was considerable, particularly in the age groups 30 to 39 and 40 to 49 years, in which the war-time rate was about one-fifth of the pre-war value. After the war the number of deaths reported from arteriosclerosis, according to official government statistics, also fell to less than half of the pre-war value.

Katila (5) has compared the possibilities of differentiating clinically between senile dementia and arteriosclerosis cerebri. In an autopsy series of 68 cases in which either or both diseases were present, he found that all (18) cases with a postmortem diagnosis of atrophia cerebri senilis were correctly diagnosed as dementia senilis. Of the cases with both senile cerebral atrophy and cerebral arteriosclerosis, both diagnoses were made intra vitam in 14 cases. In the group of cerebral arteriosclerosis (40 cases) the correct diagnoses was made only 26 times. The mean age at death of this group was 66 years, in one case only 36 years. All 40 presented neurologic symptoms and hypertension was present in every case, the mean systolic pressure being 205 mm. Hg.

A few anatomic studies deal with age changes in various organs. Uotila (16) has published data concerning the weight of the heart, spleen, liver, pancreas, kidneys, thyroid gland, and adrenals at different ages from 0 to 80 years. Sauramo (8) has measured the size of the ovaries in fetal and other age periods. Siirala (15) has examined the anatomic structure of ductus and saccus endolymphaticus in old people.

Several studies deal with demographic and medico-social topics. Kannisto (4), in a comprehensive study based on official statistics on causes of death in Finland, 1936-1940, examined the causes of death as demographic factors. He attempted to elucidate how much the elimination one by one of each of the principal causes of death would save in living years and working years, respectively, in this country.

Some of his results are as follows: Tuberculosis ranks first among the causes of death and its eradication would save 3.91 years per live birth; heart diseases occupy the second place with 2.30 years; diseases of early infancy come next with 2.19; for influenza and pneumonia, the corresponding value is 2.17; for violent death, 1.33; for cerebral hemorrhage, etc. 1.21; for cancer, 1.11. If only years of

the productive age to be saved are calculated, the ranking is altered in so far as the heart diseases drop from the second to the fifth place.

The author also endeavors to establish what he calls "the natural length of life" in Finland. For this purpose he determines the age of maximum death rate in a material, where all other causes of death are excluded, except those of senile debility. This age, i. e., the most common length of life in those persons in which the death certificate does not reveal any specific cause of death was 85 years.

Setälä (12) describes the demographic and medico-social status of a Finnish middle-south community. He studied, among other things, the age distribution in different social groups, i. e., in laborers (55 per cent of the total population) and in farmers, who comprised 37 per cent of the population. Among farmers the old age classes clearly outnumber the corresponding age group among laborers; e. g., 17 per cent of the farmers, but only 8.3 per cent of the laborers are over 60 years old; 29 per cent of the farmers were over 50, whereas the corresponding percentage was 17 for the laborers. The mean length of life exceeded by a few years that of the whole country, being 58.3 for males and 62.5 for females. Since medical service is no better in this district than elsewhere in Finland, the favorable mortality figures are obviously due to better social conditions.

Another object of the study was the incidence rate of certain specific conditions: occurence of parasitic worms, tuberculosis, and syphilis. The incidence rate of parasitic worms was shown to increase steadily with increasing age and was particularly high among the displaced persons. In the resident population, which eats less fish than the evacuées from the East of Finland, the rate of tapeworm carriers varies from 1.1 to 5.2 per cent, the lowest value corresponding to the age class 0 to 6 and 7 to 19 years, the highest to those over 60 years old. In the displaced population the incidence rate for these 7 to 19 years old is 18.1 and for those over 60 years old 36.7 per cent. Obviously the exposure to food infected with tapeworm is not the only determining factor, constitutional factors (hydrochloric acid content of the stomach?) probably being at least partly responsible for the age increase in the incidence rate.

The official statistics published at regular intervals dealing with different demographic, social, and economic topics contain, of course, many data of gerontologic interest. It is not possible, however, to review them in this connection.

E. JALAVISTO

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CORRECTION

The Journal of Gerontology has been informed by Dr. R. Altshul that the term "Feulgen-Schiff reaction" used in the abstract of his paper (volume 6, supplement to No. 3, page 56) should be "Periodic acid-Schiff reaction."

GERONTOLOGIC REVIEWS

A REVIEW OF FACILITIES AVAILABLE FOR OLDER PEOPLE

It has long been known that when the effort of the mind to grow into new knowledge and new insights ceases, the mind become fixated, settled—the pattern of arrested development.

A sign "Pioneer Club" over the door of a small building in Iron Mountain, Michigan, was largely the deciding factor in starting a search to find what older citizens are doing. What are the major problems of older people, especially in our urban centers? Are there organizations working for good adjustment and effective use of senior citizens, and what are the attitudes of civic leaders towards the need for organizations for older people?

Started as the result of a suggestion to the city council by the Mayor and assisted by the Chamber of Commerce, newspaper editor, radio station, and various individuals, the Pioneer Club represents a unique combined city movement. This social group, organized in January, 1948, when elderly men were refused the use of the local railroad station as a place to spend their time, has good potentialities for future expansion.

The opinion of the leaders is that older people today are the ones to whom they are indebted for the greatest half century of progress the world has known and that the older people are watching with great interest the progress of others in the community. The simplicity and naturalness of this assumption made the establishment of the Pioneer Club easily understood. The acceptance of the club was expressed by a 77 year old retired engineer, "It's the finest thing that has ever been done in this town. We, of the older generation, have often talked about it, but we never thought it would be done."

Methods

From these inquiries in Iron Mountain came the decision to interview other mayors and chambers of commerce for the study of older people and their activities. The purpose of the interviews was: to locate organizations of and for older people, to stimulate interest in such organizations, to create a desire for movements of this kind, and to exchange information between them.

Seventy-five interviews were made in 3 states—26 in Michigan, 24 in Indiana, and 25 in Ohio. Sampling was divided equally among 3 groups: villages with up to 10,000 population, towns up to 35,000, and cities of 35,000 and over. These 3 states were believed to be typical of industrial regions and the investigations were concerned in finding organizations serving older people.

Because no precedent could be found for gathering information on this subject from mayors and chambers of commerce, the first approach consisted in explaining the problem and developing a brief questionnaire with the help of those interviewed. Some of the best ideas came from those communities which as yet had no organized movement in this direction but which had sensed the growing need for activities for older people.

Only 4 of those interviewed felt no need to provide any assistance other than Federal Old Age Assistance for people over 65 years of age. Forty-one groups were found in 15 communities. Thirty-eight of these groups were in operation and 3 were organizing. A summary of the organizations operating in the 3 states is given in table 1. Of the 41 organizations found in the 3 states, 35 were mostly social or recreational. Five were for housing and 1 was vocational.

At the beginning of the interviews with the mayors and personnel of the chambers of commerce 90 per cent said they thought the Welfare Department would have the information

TABLE 1. ORGANIZATIONS FOR OLDER PEOPLE.

Location	Number of Organizations	Sponsors		
		Public	Religious	Private
Indiana				
Fort Wayne	3	3	0	0
New Albany	1	0	1	0
Cambridge	1	1	0	0
Winchester	1	0	0	1
Michigan				
Ann Arbor	1	1	0	0
Fenton	1	1	0	0
Greenville	1	0	0	1
Iron Mountain	1	1	0	0
Kalamazoo	1	0	0	1
Lansing	1	1	0	0
Pt. Huron	2	0	1	1
Ohio				
Bryan	1	0	0	1
Cleveland	24	6	9	9
Findlay	1	1	0	0
Norwalk	1	1	0	0
Total	41	16	11	14

Mimeographed copies of the names and sponsors of the various organizations listed in this table, together with their addresses, may be obtained from Mrs. Bernard Coggan, 624 North Hagadorn Road, East Lansing, Michigan, at 10c each.

wanted. In answer to this it was pointed out that the study was also concerned with the activities of older individuals not in need of subsistence. Whenever possible all references were followed and many interesting ideas were obtained from consultation with the Welfare Departments.

A good example of how an organization can be formed by the combined efforts of the churches of a city was a Good Will Industry for older citizens in New Albany, Indiana. Its two greatest services were to provide some occupation for older people who needed work, especially supplementary work, and to provide articles of clothing and home furnishings at moderate cost. Suitable quarters and heat were furnished by the city. Furniture and clothing were made and repaired by workers who were paid on an hourly basis. The articles were sold at the lowest possible cost. Older experienced workers trained newcomers and some handicapped workers were retrained for occupations suitable to their abilities.

There are 3 clubs in Ft. Wayne, Indiana: the Bloomington Oldsters Club, the Jefferson Center Oldsters Club, and the McCulloch Oldsters Club. The latter is part of a $62,000 Negro Community Center.

The Recreation Opportunities for Older People of Greater Cleveland, Ohio, was the most expansive and the oldest organization found. It was organized on an experimental basis forty-three years ago by the Benjamin Rose Institute. The first club started in a settlement house and later clubs were organized in churches, women's clubs, and other agencies. The Rose Institute turned the project over to the Welfare group in 1948. The aim is to have activities which provide mental stimulation, satisfactory social relations, encouragement in the acceptance of responsibilities, and the security of belonging to a group where one is wanted.

Membership is secured by names furnished by the Division of the Aged and Family Service, hospitals, and clinics, news items in daily papers—pictures and stories of activities, direct invitations to old people in the immediate neighborhood, posters in store windows, pastors of all denominations, key people of neighborhood who help with planning and suggest names, and members contacting other individuals.

Cleveland's next step was the organization of Hobby Clubs. These smaller groups are given supervision by trained leaders and are one solution to the problem of idleness among old people.

Other projects in Cleveland are the Cleveland Church Federation that sponsors worship, vesper services, and counseling service for older people, and the Women's Volunteer Committee consisting of 60 women who give four

hours each week helping at Cooley Farms, Cleveland's home for the aged and chronically infirm.

The Chamber of Commerce in Findlay, Ohio, sponsors a city-wide research to locate former members of chambers of commerce, then incorporates the experience and abilities of these older citizens when planning the present program for their city. The success of this research has influenced other civic and fraternal organizations to make use of senior members. The belief is that if older people are again to take their rightful place in the enrichment of our culture, this must be accomplished through their use in and by civic groups accepted and held in high esteem by the culture itself, whereas organizations that symbolize need, penury, and infirmity cannot do this.

One excellent housing plan was found in Norwalk, Ohio, called the Homewood Cottage Community for Older People. It consists of a group of small low rent cottages arranged around a court of lawn with a Chapel Hall at one end and a grocery nearby. The community is as self-governed as possible. Drawings of plans and more complete details are available.

In Michigan, Fenton's 5000 villagers have a modern Community Hall where a group of Golden Age people meet every two weeks for social recreation. This club has an average of 90 in attendance.

Greenville, another Michigan village of 7,500, has just appointed a City Committee of Recreation, hired a full time director, and begun a building to house the City Recreation Program on land donated by the city. This program has been scheduled to include older people.

Kalamazoo, Michigan, has a Three Quarters Century Club which started sixteen years ago and admits associate members at 60 years of age but grants active membership only after 75. Room, heat, and light are furnished by the County and meetings are held every two weeks.

An example of interracial cooperation was shown in the beginning of one Golden Age Club sponsored by the Salvation Army in Pt. Huron, Michigan. The membership of 65 is composed of 57 white and 8 non-white and the club is partially financed by the Community Chest.

Pt. Huron also has the Gratiot Memorial Home, originated five years ago through the ingenuity of 4 women who canvassed and obtained enough $100.00 donations to make a down payment on a house and lot for aged women. Most of the women guests are Old Age Pensioners. Five dollars a month of the pension are returned to them for spending money. Any deficit is paid by the Community Chest. In addition to buying this home, the sponsors have since placed more than 200 older women in private foster homes.

In the course of the interviews 3 plans were suggested for the employment of older people. These plans are now in operation on an experimental basis by individuals actively interested.

(1) The Luker Block Plan (Dr. L. Luker, Michigan State College, East Lansing, Michigan). The aims of this plan are: to have one person in each community contact mayors and chambers of commerce, business firms, religious organizations, civic and educational building managers, and others, to find occupation for older people; to estimate employment value of these individuals by time study based on normal hour output, but rigid adherence to hours not required; and to establish a centrally located office to record the work qualifications of older applicants.

(2) Sedan's Central Clearing House Plan (Secretary of the Chamber of Commerce, Mt. Clemens, Michigan). The purpose of this plan is: to establish an intercity registry of work qualifications of older applicants. This would have the effect of assisting smaller cities, which usually have insufficient funds, to obtain the best personnel, and in training younger assistants by the use of retired people from larger cities.

(3) Sternman's Screening Plan (Director

of the United States Employment, Fostoria, Ohio). The objects of this plan are: to screen all requests for help from employers in order to see if work could be done by older people; to contact employers personally in order to ascertain if older people would be acceptable; to encourage acceptance and use of older workers; and to follow up appointments in order to determine if the work has been mutually satisfactory to employer and employee.

BLANCHE B. COGGAN

BOOK REVIEWS

TERMINAL CARE FOR CANCER PATIENTS, a Survey of the Facilities and Services Available and Needed for the Terminal Care of Cancer Patients in the Chicago Area, the Central Service for the Chronically Ill of the Institute of Medicine of Chicago, 1950, 211 pages, paper bound, $1.25.

This book is a report of a survey of the facilities and services available and needed for the terminal care of cancer patients in the Chicago area undertaken by the Central Service for the Chronically Ill, through funds allocated by the Illinois Division of the American Cancer Society.

The book includes a section on the individual needs of the terminal cancer patient and a section on the services and facilities in the community which are required to meet those needs. The latter part of the book is devoted largely to a discussion of resources already available in the Chicago area and recommendations for further extension of services. Thus the book contains material of general interest to those who work with cancer patients and specific information regarding the needs of such patients based on scientific study.

The study revealed that at any given time cancer patients in need of terminal care are in a ratio of approximately one terminal care patient to every four annual cancer deaths. About 80 per cent of these patients require terminal care outside their own homes. Adequate care for terminal cancer patients costs from $5.00 to $15.00 per day, depending upon the kind of care which is needed. More than half of these patients require some financial assistance in meeting these costs.

In addition to excellent statistical tables and well summarized conclusions and recommendations, the authors have been very sensitive to the needs of the individual cancer patient. They point out that there are many common misconceptions about the terminal cancer patient, that he is not necessarily a person with an open lesion or an objectionable odor, but rather a person suffering from a terminal illness who requires personal attention and in addition various resources which his community should make available to him. The objective of his care should be to make his final days or months of life as pleasant and as bearable as possible.

The statistical method and the tables included in the book might well serve as guides for other groups anticipating such a study in other communities. The compilers of these data are careful to point out that cancer patients are not the only ones who require terminal care and that there is a need for further research in other areas of medical care.

The authors recommend that there be persistent and aggressive action by all interested agencies to improve the standards of public assistance, that medical services be extended to patients in their homes as well as in clinics and hospitals, that medical social service be used more effectively in hospitals and clinics, that more approved centers be developed for the training of practical nurses, and that housekeeping services be extended to families who are caring for terminal care patients in their own home.

The book is interesting and thought provoking. The method of study and the presentation of the data are well handled, and although findings are frequently repeated, the repetition is generally effective. Perhaps future studies will serve further to point out that terminal cancer needs to be regarded as any other illness and that the terminal cancer patient needs to be regarded as any other patient.

E. SWENGEL

ELECTROENCEPHALOGRAPHY IN CLINICAL PRACTICE, Robert S. Schwab, W. B. Saunders and Co., Philadelphia, 1951, 195 pages, $6.50.

The author of this brief treatise has selected his audience from among neurologists, internists, psychiatrists, and neurosurgeons, and avoids any implication that he is attempting a textbook sufficiently comprehensive to satisfy electroencephalographers. Thus the book differs from avaliable atlases and texts. Typography is excellent. Illustrations are simply constructed and adequate for conveying the ideas of the author. The clinical uses of electroencephalography are reliably and succinctly presented in non-technical language and are based principally upon the author's wide experience.

Reliable statistics of utilitarian interest are provided. Coverage of the EEG in Geriatrics is scanty, which is understandable considering the small interest electroencephalographers have evinced to date in that specialty of medicine.

J. L. O'LEARY

ANNOTATED BIBLIOGRAPHY OF VITAMIN E 1940 to 1950, Compiled by Philip L. Harris and Wilma Kujawski of The Research Laboratories of Distillation Products Industries, (Division of Eastman Kodak Company), Rochester 3, New York, 184 pages, $3.00.

This paper-bound volume represents a collection of abstracts of 1562 articles on vitamin E. To the interested physician, the task of keeping abreast of new developments in vitamin E research has been simplified.

The compilers are to be congratulated on their logical separation of the abstracts by content rather than by date. A table of contents includes among other topics the occurrence, chemistry, physiology, pharmacology, medical and therapeutic use, and veterinary use of vitamin E.

The compilers admit that they are more interested in the physiologic than in the medical aspects. Probably the least valuable part of the book therefore, is the section of the therapeutic use of vitamin E. For instance, the optimistic reports on vitamin E in amyotrophic lateral sclerosis are not counter-balanced by later work showing its uselessness.

R. W. STEINHARDT

RETIRE AND BE HAPPY, Irving Salomon, Greenberg, New York, 1951, 205 pages, $2.95.

This unpretentious, stimulating volume comes as close as a book usually does in meeting the task of its subtitle "The Way to Contentment for Any Man Who Retires or Who Contemplates to Do So." To make the bargain even better, it is written in a good style that avoids the technical and the pedantic and at the other extreme avoids the "cute" and condescending approach to the aged person. There is an implication throughout that the author realizes that everyone, at every age, is aging. As the pedantic might say, Salomon recognizes aging as a dynamic, not a static condition. In fact, the author sounds like a person it would be a pleasure to know and visit with—which cannot be said about just any book.

The key to the book seems to be ways and means of approaching retirement so that time will not hang heavy. This is almost a warning and it is supported by a long check-list of hobbies, ways to extend and broaden interests, sample schedules of actual week's activities, and other constructive illustrations. Salomon urges in many different ways that the person about to retire count his assets, including the non-financial, which are often the more important. He gives a number of thumbnail case sketches that are highly provocative. They are drawn from the range of wealth and "reduced circumstances" and serve as well as anything to recognize that the man who retires is not always the well-to-do. It is clear that some money

or means of support are necessary. Although the whole book is based on the premise that man cannot live by bread alone, Salomon recognizes that this statement, once uttered on the highest authority, presupposes the presence of bread.

The case sketches in the text are too brief and fragmentary to make analysis valid and it is quite possible that a few such sketches were included so that the reader can draw his own conclusions about lacks in the lives of some retired people. This is true even when Salomon does not identify the errors. For example, among the copious quotations from retired men, a few break into poetry, which in the unhabitual often means undue protestation. Some of these people might suffer from the fallacy that Salomon hits very hard: to wit, that retirement is resignation, a public admission of failing powers.

One of the most unusual and refreshing parts of the book is a chapter on the most neglected phase—"The Wife's Place in Retirement." The literature gives little enough attention to the problem of the housewife and mother who reaches the age of retirement. Retirement from what? Often from activities that she continues doing. Salomon does not pretend to go into the difficult question, but he faces the hard fact that the retirement of the husband is often very hard on the wife, who, full of love and affection and loyalty, might yet find it hard to have the fellow underfoot all the time. Salomon is gentle and perceptive in discussing this question and he gives a high rating to the wife's contribution to retirement which often imposes additional responsibilities on her.

For the record, it must be mentioned that in the appendix are check-lists of characteristics of retired men from many callings; plus a few case histories in fair detail. The analysis of these would keep a considerable amount of time from hanging heavy on the hands of the interested retired man who has a taste for this kind of inquiry.

L. TOWLEY

DIABETES MELLITUS, PRINCIPLES AND TREATMENT, Garfield G. Duncan, W. B. Saunders Co., Philadelphia, 1951, 289 pages, $5.75.

In his preface to this small volume the author states as his objectives "first, to bring together and correlate up-to-date principles in the understanding of and in the treatment for diabetes mellitus, and second, to deal with the disease and its complications in such a manner that physicians and students may find herein a practical and simplified outline of therapy." In this reviewer's opinion, both these objectives have been nicely attained.

In a foreword by F. A. Allen it becomes clear at once that among the objectives of therapy to be propounded in this volume will be the strict control of urine sugar and blood sugar. Those who treat diabetes without regard to hyperglycemia and glycosuria will find little to comfort them in this book.

The author's classification of the grades of severity of diabetes in patients who appear for treatment for the first time is useful, and will appeal, in its simplicity, to the general physician. Overweight adult diabetics who have not received insulin are considered mild cases. Markedly underweight and all child diabetics have severe diabetes. The amount of insulin a diabetic can tolerate is not an accurate measure of severity of diabetes. It thus becomes evident that restriction of caloric intake may suffice for the obese patient with uncomplicated diabetes, while the underweight patient will require insulin at the outset.

Chapters dealing with carbohydrate metabolism and the blood sugar and disturbed physiology in diabetes are short, but summarize existing knowledge excellently, and if their bibliographies are not lengthy, they are sufficient for most who will wish more information in these matters.

Chapters on the pathology of diabetes and on the symptomatology, physical signs and diagnosis of diabetes should be useful to the student and general physician. The standard glucose tolerance test (with the oral adminis-

tration of 100 gm. of glucose) is considered the best test, in doubtful cases, as to the presence or absence of diabetes. It is properly emphasized as a diagnostic aid and not as an indicator of severity of diabetes.

Treatment and insulin therapy are dealt with at length, as is proper in a volume for the general use of the man in practice. It is the author's thesis that "blood sugar values restored to and maintained within the normal range of fluctuation can have none other than a good result when wisely done." With some modifications the author's diet recommendations conform with those of The American Diabetes Association. Use of an Exchange System, adequately described, simplifies the problem of making a suitable menu from a prescribed diet. The author's recommendations as to which patients require insulin and as to choice of type of insulin are practical.

Chronic complications of diabetes and acute complications are dealt with in separate chapters, with adequate emphasis on the degenerative vascular lesions, the importance of obesity and arterial hypertension. Diseases of the coronary arteries and circulatory disturbances of the lower extremities receive special consideration. The problems of acute infections and surgery in diabetes are succinctly handled. Diabetic coma, always preventable, and always a great emergency, is considered in a separate chapter. The relation of potassium in diabetic ketosis is briefly considered.

The very special, and increasingly important problem of pregnancy complicating diabetes involves control of diabetes, adequate diet, hormonal therapy when indicated, and the wise selection of the means of terminating the pregnancy. All these items receive their fair share of discussion. The last chapter of this volume deals with the diabetic child.

Duncan is among those who advocate the strictest possible control of hyperglycemia in diabetes mellitus. There are, of course, others who feel differently. It is this reviewer's regret that, small though this volume be, the author did not allot some space in it to deal with this controversy, bringing readers up-to-date with regard to the present state of this divergence of views.

As already stated above, the objectives with which this book was written have been achieved, and it is recommended to both student and practicing clinician as a readable, practical guide in diabetes.

S. P. SCHNEIERSON

ULCUS CRURIS . ET KLINISK -ÆTIOLOGISK STUDIE MED SÆRLIGT HENBLIK PA ULCUS CRURIS POSTTHROMBOTICUM OG ULCUS CRURIS VARICOSUM (Ulcer of the Leg . A Clinical and Etiologic Study with Particular Reference to Postthrombotic and Varicose Ulcer.) H. Stürup, A. F. Hansen, Publisher, Copenhagen, 1950. 126 pages.

This monograph represents a detailed clinical study of 335 patients suffering from nonspecific ulcers of the lower leg. Of the 335 ulcer cases 130 were of postthrombotic, 148 of varicose, and 31 of arteriosclerotic etiology. The majority of the remaining 26 cases of ulcer were caused by local infections or local traumatic injury to the tissues.

The clinical symptoms in the three main groups are carefully evaluated. Most of the patients suffering from postthrombotic leg ulcer were women. In comparison with the cases of varicose ulcer there was more common occurrence of ankle edema in the postthrombotic ulcer group and more extensive tissue induration, indicating that the drainage disturbance caused by the deep thrombosis is more wide-spread and detrimental to the tissues than that caused by varicosities. The postthrombotic induration usually made its appearance before the development of the ulcer.

In the patients suffering from varicose ulcers the pathogenesis of the ulcers in the majority of the cases was pregnancy. The tissue induration in these patients usually developed after the appearance of the ulcer and seemed to be

chiefly conditioned by the ulcer itself. It was found on measurement of the venous pressure in the veins of the lower leg that patients with varicose ulcers usually showed a pronounced fall in venous pressure during walking with compression of the incompetent saphenous vein, whereas the majority of the postthrombotic ulcer patients did not exhibit any such fall in pressure during walking.

In the group of patients with arteriosclerotic leg ulcer varicosities were usually absent. The arteriosclerotic ulcers, found on all parts of the lower leg, were often multiple, and showed marked tissue induration. Only a few of the patients suffered from edema, heaviness, and fatigue, but a large proportion had pains, even during periods when the ulcer was absent.

An interesting feature of this monograph is the observations on the mean age of the patients at the time of the first appearance of the ulcers, the findings with regard to the average number of days per year the ulcers were present, and the length of absence from work caused by the ulcers. These observations can be summarized in the form of a table.

Type of ulcer	Post-thrombotic	Varicose	Arterio-sclerotic
Average age of patient at first appearance of ulcer	42.3	39.1	65.3
Duration of open ulcer, in days per year	113	56	64
Absence from work, in days per year	25	9	16

It is to be regretted that this monograph was not published in a language understandable by a wider circle of readers. The six page English summary included in the book, although fairly adequate, does not contain the many valuable details and comments made by the experienced author throughout the text.

J. E. KIRK

BOOKS RECEIVED

Books received since May 1, 1951, are acknowledged in the following list. In so far as space and time permit, some will be selected for review in a later issue, but it is unlikely that all will be reviewed.

Annual Report of the Board of Pensions, The Board of Pensions of the Presbyterian Church in the United States of America, Witherspoon Building, Philadelphia 7, Pennsylvania, 1950, 115 pages, paper bound.

Begin Now—to Enjoy Tomorrow, by Ray Giles, Mutual Benefit Life Insurance Company, Newark, New Jersey, American Book-Knickerbocker Press, Inc., 1951, 57 pages, 50¢.

Community Services to Older Jewish Persons in Dayton, Ohio. Survey Report, Council of Jewish Federations and Welfare Funds, 165 West 46 Street, New York 19, New York, 1951, 41 pages, mimeographed.

Diabetes Mellitus, Principles and Treatment, by Garfield G. Duncan, W. B. Saunders Company, Philadelphia, 1951, 289 pages, $5.75 (Reviewed in this issue, page 400).

Diseases in Old Age, by Robert T. Monroe, Harvard University Press, Cambridge, 1951, 402 pages, $5.00.

Electroencephalography in Clinical Practice, by Robert S. Schwab, W. B. Saunders Company, Philadelphia, 1951, 195 pages, $6.50 (reviewed in this issue, page 399).

Emotional Factors in Cardiovascular Disease, by Edward Weiss, Charles C Thomas, Publisher, Springfield, Illinois, 1951, 84 pages, $2.25.

Handbook of Nutrition, second edition, by George Cowgill, William J. Darby, Charles Davidson, C. A. Elvehjem, Morris Fishbein, Phillip C. Jeans, Howard B. Lewis, James S. McLester, Harold C. Stuart, Russell M. Wilder, John Youmans, and James Wilson, The Blakiston Company, Philadelphia, 1951, 717 pages, $4.50.

Hope and Help for the Alcoholic, by Harold W. Lovell, Doubleday & Company, Inc., New York, 1951, 215 pages, $2.75.

The Integration of Psychiatry and Medicine, by William B. Terhune, Grune & Stratton, Inc., New York, 1951, 177 pages, $2.75.

An Introduction to Modern Psychology, by O. L. Zangwill, Philosophical Library, New York, 1950, 227 pages, $3.75.

Personnel Administration in Public Health Nursing, by William Brody, C. V. Mosby Company, St. Louis, 1951, 209 pages, $3.75.

Retire and Be Happy, by Irving Salomon, Greenberg Publisher, New York, 1951, 205 pages, $2.95 (Reviewed in this issue, page 399).

Skill and Age, An Experimental Approach, by A. T. Welford, Oxford University Press, New York, 1951, 161 pages, $1.75.

Survey of the Needs of Jewish Aged Persons, New York City, 1949, with Recommendations for a Comprehensive Community Plan, by the Professional Committee, Central Bureau for the Jewish Aged, Inc., New York, 1950, 50 pages, 11 pages appendix, mimeographed.

Symposium on Steroids in Experimental and Clinical Practice, edited by Abraham White, The Blakiston Company, New York, 1951, 415 pages, $7.50.

Ulcus Cruris. Et klinisk -ætiologisk Studie med særligt Henblik på Ulcus cruris postthromboticum og Ulcus cruris varicosum (Ulcer of the Leg. A Clinical and Etiological Study with Particular Reference to Postthrombotic and Varicose Ulcer), by H. Stürup, A. F. Hansen, Publisher, Copenhagen, 1950, 126 pages, (Reviewed in this issue, page 401).

Vitamin E: Annotated Bibliography 1940 to 1950, by Philip L. Harris and Wilma Kujawski, the National Vitamin Foundation, Inc., New York, 1951, 184 pages, $3.00, paper bound, (Reviewed in this issue, page 399).

INDEX TO CURRENT PERIODICAL LITERATURE

NATHAN W. SHOCK
Gerontology Section
National Heart Institute
National Institutes of Health

The subject categories are those in *A Classified Bibliography of Gerontology and Geriatrics* by Nathan W. Shock published by Stanford University Press, Stanford, California (1951). Only major headings are used and the Roman numerals correspond to those given in the bibliography. In so far as possible, references are classified according to organ systems. Thus most of the material on Geriatrics will be found under the organ system involved in the disease. Cross references are indicated by number at the end of each section. When available, abstract references are given *(B.A.—Biological Abstracts; P.A. — Psychological Abstracts; and P.I.—Population Index).* Abbreviations for journals are those used in *A World List of Scientific Periodicals Published in the years 1900-1933,* 2nd Edition. For journals not listed, abbreviations were devised according to the general rules used in the above source. It is impossible to cover all journals and list all papers concerned with aging and the aged. Authors and publishers are requested to call attention to publications or to send reprints to the Gerontology Section, Baltimore City Hospitals, Baltimore, Maryland. The assistance of the Forest Park Foundation, Peoria, Illinois, in the preparation of these materials is gratefully acknowledged.

GERONTOLOGY

3944. Bortz, E. A.: Biology of aging. *Delaware St. med. J., 23:* 112-116, 1951.

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3946. Hirsch, S.: Origines, principes et buts de la Gérontologie contemporaine. *Brux. méd., 31:* 179-186, 1951.

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3948. Shock, N. W.: The age problem in research workers. Physiological viewpoint. *Sci. Mon., N. Y., 72:* 353-355, 1951.

3949. Thomson, A. P., —. Amulree, and F. G. W. Marson: Discussion of the problems of old age. *Proc. roy. Soc. Med., 43:* 929-936, 1950.

3950. Thurston, J. L.: National committee on aging and geriatrics. *Geriatrics, 6:* 117-118, 1951.

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3953. U. S. Bureau of Old-Age and Survivors Insurance. Division of Program Analysis: *Annotated bibliography on problems of the aging.* The Bureau, Baltimore, 1951, 49 pp.

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